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## Research Article

# Comparison of Efficiency of Two Different Mouth Washes of Complementary and Alternative Medicine Source with Chlorhexidine Mouth Wash-A Randomized Control Trial

Ashok KP, UVVSSS Jagannadha Raju, Manikanta Kumar SS, Anupama M, Lakshmi Soumya M

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### ABSTRACT:

**Background-** Plaque control and removal of bacterial biofilm are essential components in preventing and treating gingival disease. Mouthwashes improve oral health care by inhibiting bacterial adhesion, colonization, and metabolic activity. The study was aimed to assess and compare the plaque formation, gingival inflammation, and gingival bleeding.

**Materials & Methods-** The study was designed as a randomized clinical study where clinical parameters such as gingival index, plaque index, and modified sulcular bleeding index were recorded immediately and 15 days after oral prophylaxis. The subjects in this study included 80 gingivitis patients who are divided into four groups of 20 patients in each group. Group A was given chlorhexidine mouthwash, group B was given Hiora, group C was given Perio Aid and group D was given distilled water.

**Results-** In each of the study groups, there was a significant reduction in gingival, plaque, and modified sulcular bleeding index scores from baseline to 15 days. The chlorhexidine group demonstrated significantly lesser mean gingival, plaque, and modified sulcular bleeding index scores compared to all other three groups.

**Conclusion-** Within the limits of this study, it can be concluded that all three types of mouthwashes are effective in reducing dental plaque and gingivitis adjunctive to scaling. Herbal mouthwashes are comparable to chlorhexidine in terms of plaque reduction and reduction of gingival inflammation.

**KEYWORDS:** Hiora, Perioaid, Chlorhexidine, Plaque index, Gingival index.

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### INTRODUCTION:

GINGIVITIS is an inflammatory reaction to a dental plaque whereas Periodontitis is a destructive inflammatory disease of the supporting tissues of the tooth resulting in progressive destruction of the periodontal ligament, and alveolar bone with pocket formation and recession.<sup>[1]</sup> Periodontal disease is induced by bacterial infections in which microbial plaque plays a crucial role. Plaque control and removal

of bacterial biofilm are essential components in the prevention and treatment of periodontal disease.<sup>[1]</sup> Plaque reduction has been the hallmark of preventive dentistry since the advent of antibiotics and the realization that bacteria are possible causative agents of the major dental diseases, caries and periodontal disease.<sup>[1]</sup> Dental plaque biofilm cannot be eliminated permanently. The pathogenic nature of dental plaque

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biofilm can be reduced by reducing the total microbial load. Both chemical and mechanical oral hygiene aids are used for removal and prevention of plaque. Even though the toothbrush is the most widely used oral hygiene aid, a majority of the population is not able to perform mechanical plaque removal effectively.<sup>[2]</sup> Hence, there is a need for chemical plaque control. Chemical methods of reducing plaque, such as mouthwashes, are therefore appealing as they can provide significant benefits to patients.<sup>[3]</sup> These are simple and widely accepted method to deliver the antimicrobial agent (after toothpastes), which can be used by the patient as an oral hygiene aid. Various mouth rinses are available in the market, amongst which Chlorhexidine is the most popular. It is recognized as the primary agent for chemical plaque control, its clinical efficacy being well known to the profession.<sup>3</sup> But it cannot be used on a long-term basis because of various side effects like brown discoloration, taste perturbation, oral mucosal lesions, parotid swelling, enhanced supragingival plaque formation and sometimes unacceptable taste. Given the advantages of herbal compounds and their fewer side effects compared to their chemical counterpart, herbal mouthwashes are considered as a viable alternative to chlorhexidine mouthwash.<sup>[4]</sup> HIORA is phytopharmaceutical dental preparation to maintain and enhance oral hygiene by providing antiseptic, refreshing and antimicrobial properties.<sup>[1]</sup> PERIOAID contain *Calendula officinalis* which works as a remarkable healing agent and consists of triterpenoids which are important anti-inflammatory and anti-edematous components in plant. Taking into consideration the side-effects of chlorhexidine, and the penchant of people for herbal/natural products, the present study was conducted with an aim to compare the anti-plaque efficacy of 0.2% chlorhexidine gluconate mouthwash and the herbal mouthwashes such as Hiora and Perioaid with distilled water as control.

## MATERIALS & METHODS:

This study was undertaken in the outpatient at the Department of Periodontics, GSL Dental College, Andhra Pradesh, India. The study sample consisted of 80 patients who were diagnosed as having gingivitis. They were randomly divided into four groups, Group A, B, C and D. Group A patients were prescribed with Chlorhexidine mouthwash, Group B patients were prescribed with Hiora mouthwash, Group C patients prescribed with Perioaid and Group D prescribed with distilled water. Patients having systemic disease, pregnancy, and who were undergoing antimicrobial therapy were excluded from the study. The study was

presented to the Institutional Scientific Review Board and got approved. Informed consent was obtained from the patients after explaining the details of the study.

## Study procedure:

This study was designed as a double-blind, randomized, control trial comparing the efficacy of three mouthwash solutions. In this study, eighty patients of age group between 18-25 years were selected through purposive sampling and then were randomly divided into four groups: the chlorhexidine group (n =20), Hiora group(n=20), Perioaid group(n=20) and the distilled water group (n = 20). The demographic data such as name, age, and gender were collected for each patient in all the four groups. Clinical assessments were performed by examiner A (Jagannadha Raju) using mouth mirror and probe. Oral prophylaxis was not performed so that the study could begin with the existing oral hygiene status of the subjects. Pre-operative measurements were recorded which included gingival index (GI), plaque index (PI) and modified sulcular bleeding index (mSBI). Oral prophylaxis was performed after the initial clinical assessment. After oral prophylaxis, the patients were then prescribed a mouthwash based on their respective categorized group by Examiner B (Ashok KP). Examiner A was not aware of the mouthwash prescribed to the patient. 0.2% chlorhexidine mouth wash was given to group A. They were asked to use 10 ml 2 times a day in an interval of 12 hours for 15 days and instructions were given not to rinse their mouth for half an hour. Hiora (ayurvedic mouth wash) was given to group B and they were asked to use 10ml twice daily in an interval of 12 hours for 15 days and instructions were given not to rinse their mouth for half an hour. Perioaid (homeopathic mouth wash) was given to group C and they are asked to use 6 drops in ¼ th cup of water twice daily in an interval of 12 hours for 15 days and instructions were given not to rinse their mouth for half an hour. Distilled water was given to group D and they are asked to use twice daily in an interval of 12 hours for 15 days and instructions were given not to rinse their mouth for half an hour. The labels were removed from the bottles before they were given to the patients. The patients were asked to report to the clinic after 15 days from the date of the initial examination. Examiner A, who was trained and calibrated to record the plaque, gingival and bleeding index scores, recorded the findings at both intervals and for all the four groups. Examiner A was blinded to the type of the mouthwash used by participants. The collected data were subjected to statistical analysis.



**Table 1:** Comparison of gingival index scores at baseline and 15 days between the study groups.

Time	Group	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		<i>f</i> -value	<i>p</i> -value
						Lower Bound	Upper Bound		
Baseline	Chlorhexidine	20	1.03	0.40	0.09	0.84	1.22	3.11	0.071
	Hiora	20	0.98	0.25	0.06	0.76	1.00		
	Perioaid	20	1.04	0.35	0.08	0.87	1.20		
	Control	20	1.24	0.45	0.10	1.03	1.45		
15 days	Chlorhexidine	20	0.41	0.34	0.07	0.25	0.56	8.01	<0.001 *
	Hiora	20	0.53	0.27	0.06	0.40	0.65		
	Perioaid	20	0.61	0.29	0.06	0.48	0.75		
	Control	20	0.87	0.34	0.07	0.71	1.02		

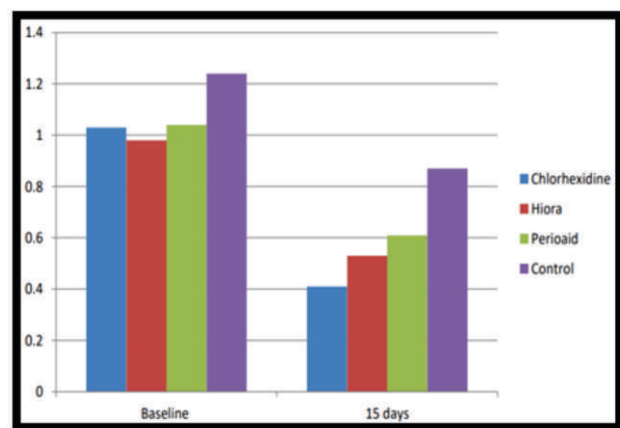
One way analysis of variance;  $p \leq 0.05$  considered statistically significant; \* denotes significance

### STATISTICAL ANALYSIS:

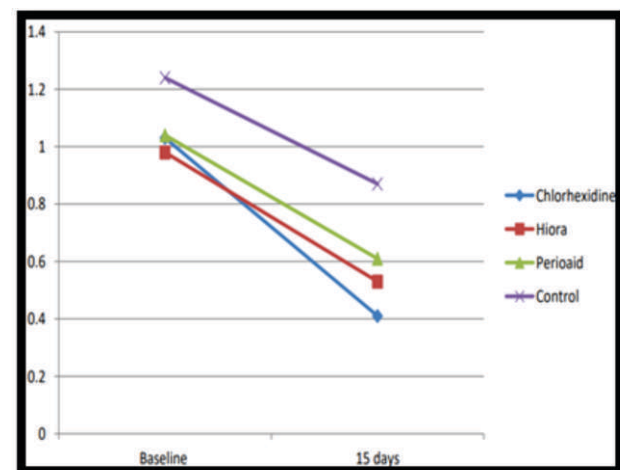
Data were analyzed using IBM SPSS version 20 software. Descriptive statistics, one-way analysis of variance, and paired t-tests were done to analyze the study data. Bar charts and line diagrams were used for data presentation.

### RESULTS:

Gingival index scores of the patient at baseline and 15 days among four different study groups state that there was significant difference with chlorhexidine group showing greater reduction in mean values from 1.22 at base line to 0.56 after 15 days compared to other three study groups (Table 1; Figure 1). The plaque index scores of the patient at baseline and 15 days among four different study groups state that there was significant difference with chlorhexidine showing greater reduction in mean value from 1.48 at base line to 0.47 after 15 days compared to other three study groups with least reduction seen in control group where mean reduction value seen from 1.72 at base line to 1.26 after 15 days (Table 2 ; Figure 2). Modified sulcular bleeding index scores of the patients among the four different study groups establish that there was significant difference with chlorhexidine showing greater reduction in mean values from 0.77 at base line to 0.18 after 15 days compared to other three study groups with least reduction seen in control group with mean values from 0.71 at base line to 0.53 after 15 days (Table 3 ; Figure 3). Intra group comparison of gingival index, plaque index and modified sulcular bleeding index scores between baseline and 15 days in each of the study groups demonstrate that mean values were found to be significantly lower than the pre-operative mean values. At the end of 15 days, almost comparable reduction in the amount of plaque and gingivitis was



**Figure 1:** Comparison of gingival index scores at baseline and 15 days between the study groups.



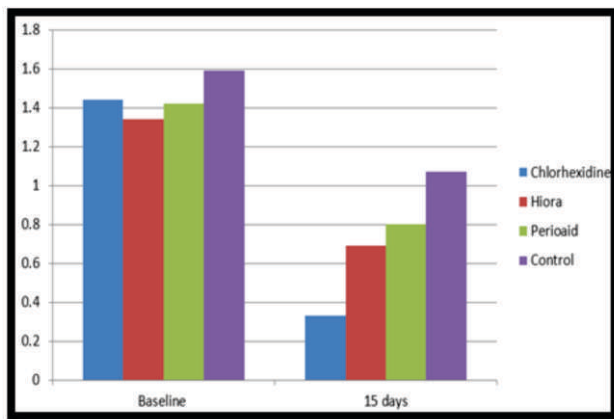
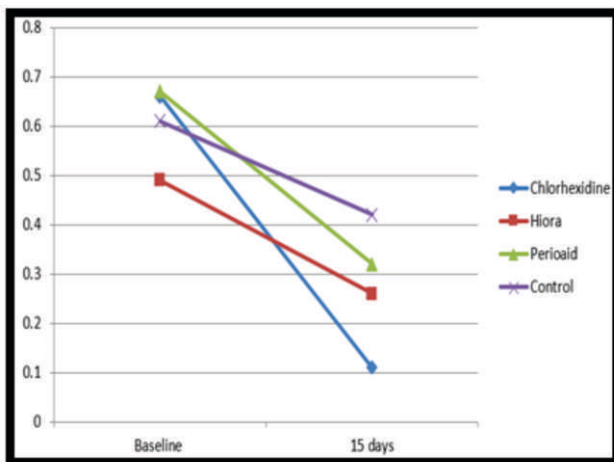
**Figure 2:** Comparison of plaque index scores at baseline and 15 days between the study groups.

found in all the four groups (Table 4,5,6 ; Figure 4,5,6). There were no significant differences in mean gingival, plaque, and modified sulcular bleeding index scores at baseline between the study groups.

**Table 2:** Comparison of plaque index scores at baseline and 15 days between the study groups.

Time	Group	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		f-value	p-value
						Lower Bound	Upper Bound		
Baseline	Chlorhexidine	20	1.44	0.31	0.07	1.29	1.58	7.63	0.079
	Hiora	20	1.34	0.32	0.07	0.99	1.29		
	Perioaid	20	1.42	0.32	0.07	1.27	1.58		
	Control	20	1.59	0.27	0.06	1.46	1.72		
15 days	Chlorhexidine	20	0.33	0.30	0.07	0.19	0.47	15.93	<0.001 *
	Hiora	20	0.69	0.37	0.08	0.51	0.86		
	Perioaid	20	0.80	0.25	0.06	0.68	0.92		
	Control	20	1.07	0.41	0.09	0.87	1.26		

One way analysis of variance;  $p \leq 0.05$  considered statistically significant; \* denotes significance

**Figure 3:** Comparison of modified sulcular bleeding index scores at baseline and 15 days between the study groups.**Figure 4:** Comparison of gingival index scores between base line and 15 days in each of the study groups.

At the 15 days follow-up, chlorhexidine group demonstrated significantly lesser mean gingival, plaque and modified sulcular bleeding index scores. In each of the study groups, there was a significant

reduction in the mean values of gingival, plaque, and modified sulcular bleeding index scores from baseline to 15 days.

## DISCUSSION:

Maintenance of good oral hygiene is the key to the prevention of dental disease. Several researchers have suggested the application of chemotherapeutic agents as adjuncts to mechanical plaque control. Furthermore, chemical agents have the ability to reach the interproximal areas that are difficult to clean and inhibit bacterial growth and subsequent biofilm formation on the soft tissue.<sup>[2]</sup> Application of these chemical agents is safe and seems to have no effect on increasing resistant species.<sup>[5]</sup>

Chlorhexidine gluconate has a broad spectrum of antibacterial effects because of its bactericidal and bacteriostatic activity and its high oral substantivity.<sup>[6,7]</sup> Chlorhexidine binds to the phospholipids in the inner cell membrane of the bacterial cell wall and leads to leakage of lesser molecular weight components and sublethal reversible bacteriostatic action.<sup>[8]</sup> In the present study, reduction in amount of plaque was found to be statistically significant in chlorhexidine group. This well corroborates with the results obtained in the previous studies carried out by Léo, and Lang et al., and Sharma et al. also found significant amount of plaque reduction in the children who used 0.2% chlorhexidine mouthwash.<sup>[9,10,11]</sup>

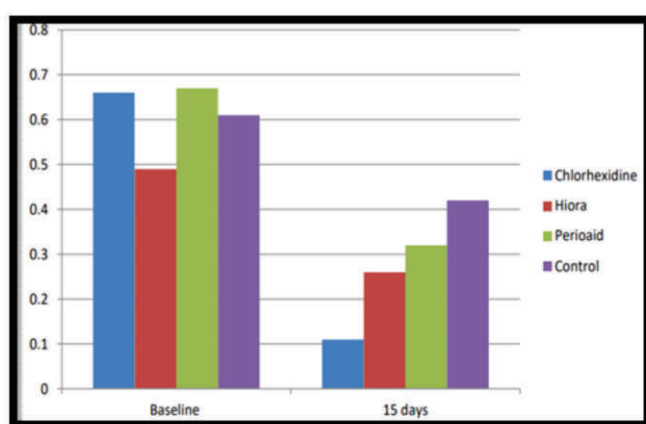
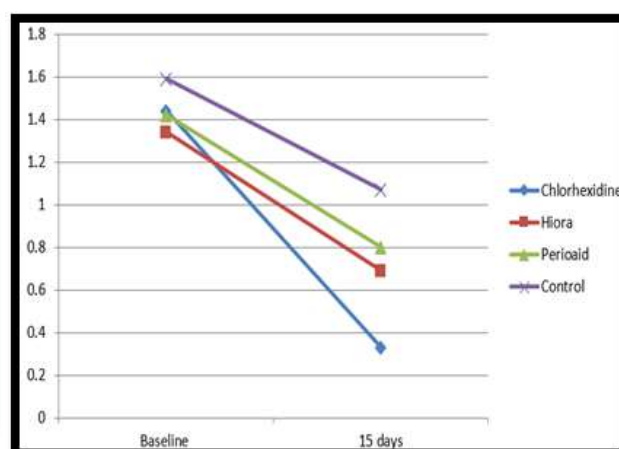
PERIOAID contains Polysaccharides which demonstrated strong bio-adhesion to buccal membranes when compared to dextran and 9 other plant extracts. They decrease local inflammation by shielding tissue from irritants and facilitating tissue hydration.<sup>[12]</sup> also contains ECHINACEA



**Table 3:** Comparison of modified sulcular bleeding index scores at baseline and 15 days between the study groups.

Time	Group	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		f-value	p-value
						Lower Bound	Upper Bound		
Baseline	Chlorhexidine	20	0.66	0.23	0.05	0.56	0.77	2.31	0.082
	Hiora	20	0.49	0.30	0.07	0.35	0.63		
	Perioaid	20	0.67	0.23	0.05	0.56	0.77		
	Control	20	0.61	0.21	0.05	0.51	0.71		
15 days	Chlorhexidine	20	0.11	0.15	0.03	0.04	0.18	7.19	<0.001 *
	Hiora	20	0.26	0.24	0.05	0.14	0.37		
	Perioaid	20	0.32	0.25	0.05	0.20	0.43		
	Control	20	0.42	0.22	0.05	0.32	0.53		

One way analysis of variance;  $p \leq 0.05$  considered statistically significant; \* denotes significance

**Figure 5:** Comparison of plaque index scores between base line and 15 days in each of the study groups.**Figure 6:** Comparison of modified sulcular bleeding index scores between baseline and 15 days in each of the study groups.**Table 4:** Comparison of gingival index scores between baseline and 15 days in each of the study groups.

Time	Group	N	Mean	Std. Deviation	Std. Error	t-value	p-value
Chlorhexidine	Baseline	20	1.03	0.40	0.09	8.16	<0.001 *
	15 days	20	0.41	0.34	0.07		
Hiora	Baseline	20	0.98	0.25	0.06	6.18	<0.001 *
	15 days	20	0.53	0.27	0.06		
Perioaid	Baseline	20	1.04	0.35	0.08	5.68	<0.001 *
	15 days	20	0.61	0.29	0.06		
Control	Baseline	20	1.24	0.45	0.10	6.38	<0.001 *
	15 days	20	0.87	0.34	0.07		

Paired t test;  $p \leq 0.05$  considered statistically significant; \* denotes significance

ANGUSTIFOLIA which stimulates the immune system to help fight infections.<sup>[13]</sup> Alkamides within echinacea help in reducing oxidative stress over the cell and work as an antioxidant to reduce inflammation. This is likely safe for most people using it in the short term.<sup>14</sup> According to a study by Safarabadi et al in

2017, comparing the Effect of Echinacea and Chlorhexidine Mouthwash on the Microbial Flora of Intubated Patients Admitted to the Intensive Care Unit stated that the echinacea solution was more effective in decreasing the oral microbial flora of patients in the intensive care unit. Given the benefits of the

**Table 5:** Comparison of plaque index scores between baseline and 15 days in each of the study groups.

Time	Group	N	Mean	Std. Deviation	Std. Error	t-value	p-value
Chlorhexidine	Baseline	20	1.44	0.31	0.07	13.62	<0.001 *
	15 days	20	0.33	0.30	0.07		
Hiora	Baseline	20	1.34	0.32	0.07	6.36	<0.001 *
	15 days	20	0.69	0.37	0.08		
Perioaid	Baseline	20	1.42	0.32	0.07	11.43	<0.001 *
	15 days	20	0.80	0.25	0.06		
Control	Baseline	20	1.59	0.27	0.06	7.03	<0.001 *
	15 days	20	1.07	0.41	0.09		

Paired t test;  $p \leq 0.05$  considered statistically significant; \* denotes significance

**Table 6:** Comparison of modified sulcular bleeding index scores between baseline and 15 days in each of the study groups.

Time	Group	N	Mean	Std. Deviation	Std. Error	t-value	p-value
Chlorhexidine	Baseline	20	0.66	0.23	0.05	10.89	<0.001 *
	15 days	20	0.11	0.15	0.03		
Hiora	Baseline	20	0.49	0.30	0.07	5.43	<0.001 *
	15 days	20	0.26	0.24	0.05		
Perioaid	Baseline	20	0.67	0.23	0.05	9.14	<0.001 *
	15 days	20	0.32	0.25	0.05		
Control	Baseline	20	0.61	0.21	0.05	6.11	<0.001 *
	15 days	20	0.42	0.22	0.05		

Paired t test;  $p \leq 0.05$  considered statistically significant; \* denotes significance

components of the herb Echinacea, it can be suggested as a viable alternative to chlorhexidine.<sup>[15]</sup> The reduction in amount of plaque in the present study well corroborated with results obtained in this study.

HIORA contains *Salvadora persica*, Naga Valli, Pilu and Peppermint. *Salvadora persica* improves gingival health and inhibits growth of cariogenic bacteria.<sup>[16,17]</sup> Naga Valli (*Piper Betle*) shows anti-inflammatory, anti-oxidant, anti-microbial properties.<sup>[18]</sup> Pilu (*Salvadora persica*) shows anti-oxidant activity. It has peppermint that contains menthol, which activates cold-sensitive TRPM8 receptors in mucosa and it is also used as primary agent in toothpastes and chewing gums, peppermint.<sup>[19]</sup> In a study conducted by Bagchi S & Saha S in year 2015, 90 nursing students were evaluated for efficiency of herbal mouth wash by Double blinded parallel randomized controlled trial technique. They were divided into three groups where group A was given chlorhexidine, group B was given Hiora mouth wash and group C was given distilled water. There was statistically significant

reduction in plaque and gingival score from baseline to 21 days and no improvement seen in group C which was done using distilled water.<sup>[20]</sup> The results of present study were also similar. A study by Bioschi (2013) states that herbal and chlorhexidine mouthwash are equally effective in vitro suggesting that herbal mouthwashes may be used therapeutically in the future to inhibit microbial growth.<sup>[21]</sup> A study was conducted by Parwani et al. where 90 patients were divided into three groups with 30 patients in each group, namely: Normal saline group, Chlorhexidine group, and Hiora mouthwash group.<sup>[22]</sup> The results showed Chlorhexidine and Hiora mouthwash were superior to normal saline, but between Chlorhexidine and Hiora group there was non-significant improvement indicating Hiora mouth wash can be viable alternative for chlorhexidine. In the present study, the reduction in amount of plaque in hiora group well corroborates with the results obtained in this study done by Parwani et al. There was a significant difference in the reduction of dental plaque in all the four groups before and after the experimental period.

Chlorhexidine shows more reduction in dental plaque, gingival and bleeding scores compared to other three mouthwashes.

### Limitations:

The present study was a short-term study employing commercially available mouth rinses. Though significant results were obtained, long-term clinical efficacy (6 months—as prescribed by ADA) and adverse effects associated with long-term usage could not be assessed. Microbiological assessment on the plaque or saliva of the participants was not performed.

### CONCLUSION:

With in the limitations of the study, it can be concluded that all three mouth washes are effective in the treatment of gingivitis when used as an adjunct to oral prophylaxis. The herbal mouthwashes are comparable to chlorhexidine in terms of plaque reduction and reduction of gingival inflammation. Further, long-term research needs to be done to check the efficacy and effectiveness of these mouthwashes over standard drug regimes.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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## Research Article

# Comparison of Ki-67 Expression in Leukoplakia and Squamous Cell Carcinoma-A Retrospective Study

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### ABSTRACT:

**Background:** Oral malignancy is the most common malignancy worldwide. In India, approximately 77000 new cases are diagnosed and 52000 deaths are reported annually.

Absolutely, understanding the molecular pathogenesis of conditions like oral leukoplakia can indeed be a game-changer in terms of early diagnosis and prognosis. Cell proliferation, which is tightly regulated in healthy tissues, can go haywire in cancer, leading to uncontrolled growth and tumor formation. By studying the molecular mechanisms underlying this dysregulation, researchers can identify potential biomarkers for early detection and develop targeted therapies to intervene in the progression of the disease. In the present study Ki-67 expression was compared between lesions of leukoplakia and Oral squamous cell carcinoma. Grades of epithelial dysplasia and Oral squamous cell carcinoma were also evaluated.

**Materials & Methods:** This retrospective study conducted at our institution, represents a significant effort to understand the proliferative activity in oral lesions. With a total sample size of 135, including 72 oral leukoplakia samples, 50 oral squamous cell carcinoma samples, and 13 normal mucosal samples, it provides a comprehensive view of Ki-67 expression in different oral conditions.

**Results:** The finding of over expression of Ki-67 with increasing grades of Oral Epithelial Dysplasia and in Oral Squamous Cell Carcinoma compared to normal mucosa was significant ( $p$ -value<0.05) and aligns with the known biology of these conditions.

**Conclusion:** The conclusion drawn from our study suggests that Ki-67 expression could indeed serve as a reliable marker for predicting the future outcome of Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma.

**KEYWORDS:** Ki-67, epithelial dysplasia, carcinoma, leukoplakia

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### INTRODUCTION:

Indeed, head and neck cancers represent a significant public health challenge worldwide. These cancers can affect various areas of the head and neck, including the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, and salivary glands. The rise in the

number of new cases each year adds to the burden faced by individuals, families, healthcare systems, and society as a whole<sup>[1,2]</sup>.

The burden of oral cancer in nations undergoing economic transition, such as India, is indeed a significant public health challenge. India, in particular, faces a substantial number of new cases and

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deaths from oral cancer each year, highlighting the urgent need for effective prevention, early detection, and treatment strategies. Approximately 77,000 new cases and 52,000 deaths annually are staggering and underscore the magnitude of the problem in India<sup>[3,4]</sup>.

Absolutely, tobacco use, alcohol consumption, and exposure to environmental carcinogens are indeed major risk factors associated with oral cancers<sup>[5,6,7,8]</sup>.

Oral pathologists play a crucial role in the early detection and prevention of oral cancers. Their unique position allows them to identify potentially cancerous lesions in the symptomless phase, often before patients are even aware of any abnormalities. This early detection is key because oral cancers, when diagnosed at an early stage, are more treatable and have a better prognosis. However, many patients may not fully understand the seriousness of oral cancers or may delay seeking medical advice due to various reasons, including lack of awareness, fear, or stigma associated with cancer diagnosis. This delay in seeking medical attention can allow the disease to progress rapidly, making treatment more challenging and reducing the chances of a successful outcome. To address this issue, oral pathologists can play a proactive role in raising awareness about the importance of regular oral screenings and early detection of oral cancers. By educating their patients about the risk factors associated with oral cancers, the signs and symptoms to watch out for, and the benefits of early intervention, oral pathologists can empower individuals to take charge of their oral health and seek timely medical advice if needed. Oral leukoplakia (OL) is one of the most common precancerous lesions<sup>[9,10]</sup>.

Leukoplakia is defined as “A white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer”<sup>[11]</sup>.

Absolutely, advancements in molecular biology have significantly contributed to our understanding of the molecular pathogenesis of oral cancer and have led to the development of newer diagnostic and treatment techniques. Molecular studies have unraveled the intricate mechanisms underlying the development and progression of oral cancer, shedding light on molecular pathways, genetic mutations, and aberrant cellular signaling that drive carcinogenesis.

One key aspect of this progress is the identification and characterization of tumor markers. Tumor markers are substances that can be detected in the blood, urine, tissue samples, or other bodily fluids of patients with cancer. These markers are often proteins or genetic materials that are either produced by

cancer cells themselves or released by the body in response to the presence of cancer.

The detection and analysis of tumor markers hold immense potential in the diagnosis, prognosis, and treatment of oral cancer<sup>[12,13]</sup>.

It is hypothesized that Cancer is characterized by uncontrolled cell proliferation, which means that cells divide and multiply at an abnormal rate, leading to the formation of tumors<sup>[14]</sup>.

Ki-67 is indeed an excellent marker for assessing the growth fraction or proliferative activity of a given cell population. Its presence throughout the active phases of the cell cycle—G1, S, G2, and mitosis—makes it a reliable indicator of cells that are actively dividing and proliferating.

Since Ki-67 is absent in resting cells (G0 phase), it provides a dynamic snapshot of the proportion of cells within a population that are actively cycling at any given time. This information is crucial for understanding the proliferative status of tissues, assessing the aggressiveness of tumors, and predicting their behavior.

In research and clinical settings, immunohistochemical staining for Ki-67 is commonly used to quantify the proliferative index or labeling index of tumor cells. By measuring the percentage of cells expressing Ki-67 in a tissue sample, researchers can estimate the rate of cell proliferation and correlate it with various clinical parameters, such as tumor grade, stage, and prognosis<sup>[15]</sup>.

We Compared Ki-67 expression levels between lesions of OL, oral squamous cell carcinoma (OSCC), and normal oral mucosa (OM). Utilizing immunohistochemistry to assess Ki-67 expression allows for a quantitative analysis of the proliferative activity within these tissue samples.

## MATERIALS & METHODS

This study was done in our institute. The study included 135 samples in total. Out of these, 72 were known OL samples, while 50 were known OSCC. 13 normal mucosal samples were taken. The normal samples were obtained from patients undergoing third molar extractions, they were informed and their approval was sought. Institutional ethical clearance for the study was obtained. The formalin fixed paraffin embedded (FFPE) tissue blocks were obtained from the department of Oral Pathology.

The blocks were sectioned at 4 micron thickness. 2 sets of slides were made, 1 for Hematoxylin & Eosin (H&E) and the other for Ki-67. Gelatin chrome coated slides were used for proper adherence of tissue sections. The slides were stained

**Table 1:** Gender distribution of the samples.

Gender	Oral Leukoplakia		Oral Squamous cell carcinoma	
	No. of patient S (n)	Percentage (%)	No. of patient S (n)	Percentage (%)
Male	65	90.27	45	90
Female	07	9.72	05	10
n	72	100	50	100

**Table 2:** Distribution of cases according to dysplasia in OL

Group	Histopathological grading	No. of samples (n)	Percentage (%)
I	Mild epithelial dysplasia	30	41.66
II	Moderate epithelial dysplasia	23	31.94
III	Severe epithelial dysplasia	19	26.38

with H&E. This was followed by immunohistochemical evaluation (Ki-67). Antigen retrieval was done by placing sections in pressure cooker containing 1 mM EDTA buffer (pH 8.0) heated to 130°C for 2.5 min and then cooled to room temperature. The endogenous activity was blocked by using 0.6% methanol Hydrogen peroxide for 15-20 minutes. This was followed by rinsing with distilled water and tris buffer wash (pH 7.2-7.6). The slides were inserted in a petridish containing citrate buffer and placed in a microwave oven at 700 watts for 10 minutes. The petridish was allowed to cool to room temperature for 20 minutes and then the slides were taken out and washed with tris buffer. Excess buffer was washed and finally sections were covered with optimally diluted primary antibody and incubated at room temperature for 1 hour. After washing in wash buffer, excess was removed and this was followed by treatment with biotinylated rabbit anti mouse IgG and incubated for 30 minutes. Again the slides were washed with buffer. Enough drops of streptavidin peroxidase were applied to cover the slides and were incubated for 45 minutes. Freshly prepared substrate chromogen solution was applied to cover the sections and incubated at room temperature for 6-7 minutes. Finally, the slides were counterstained with Harri's hematoxylin. The sections were dehydrated, cleared and mounted in DPX (Distrene Debutyl-Pthalate Xylene)<sup>[16]</sup>.

## INTERPRETATION:

Histopathological diagnosis was confirmed in H&E stained sections. This was followed by analyzing

immunohistochemically stained sections for Ki-67 at different magnifications. Random 10 fields were used for the quantitative assessment of Ki-67 positive cells at high power. Intranuclear light brown granular staining confirmed ki-67 positivity. Expression of Ki-67 less than 10% were considered negative.

## RESULTS:

This study carried out in our institute was planned to correlate the ki-67 expression with histopathological grades of OSCC and OL. In a total of 72 OL, 65 were males and only 7 were females and out of 50 OSCC, 45 were males and 5 were females [Table1]. Out of 72 OL samples, 30 were mild dysplasia (Group I), 23 moderate dysplasia (Group II) and 19 severe dysplasia (Group III) [Table-2]. Similarly, out of 50 OSCC samples, 30 were well differentiated (Group IV), 15 were moderately differentiated and 4 were poorly differentiated. Since poorly differentiated were very few they were clubbed with moderately differentiated and comprised of Group V (n=20). 13 samples from normal patients formed Group VI [Table 3]. The evaluation of the slides was done by scanning the immunohistochemically stained slides and counted in five different histological fields using a magnification of 40X. An eyepiece grid was used to prevent the overlapping of fields. Comparisons were made between Group I, II and III each with Group VI. Similarly, Group IV and V were compared with Group VI. Histological grades of dysplasia in OL were also compared with histological grades of OSCC. The indices were calculated as the percentage of positively

**Table 3:** Distribution of cases according to histopathological grading in OSCC.

Group	Histopathological grading	No. of samples (n)	Percentage (%)
I	Well differentiated squamous cell carcinoma	30	60
II	Moderately & Poorly differentiated squamous cell carcinoma	20	40

**Table 4:** Comparison of Grades of OL with normal mucosa.

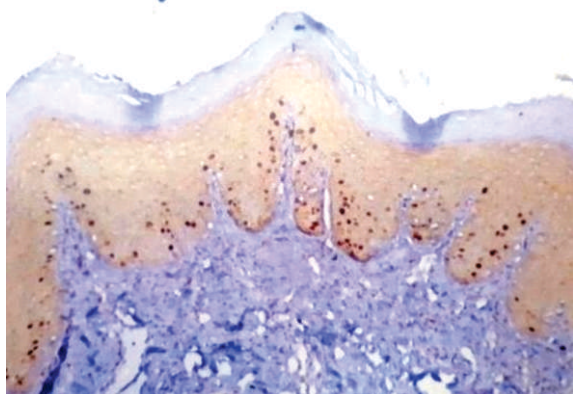
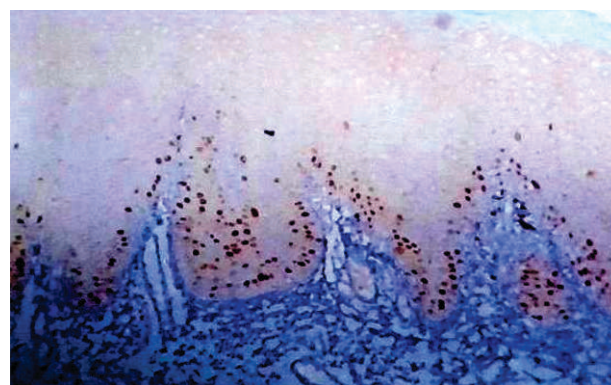
Control group n=13 [Group VI]	Mild epithelial dysplasia n=30 [Group I]	Moderate epithelial dysplasia n=23 [Group II]	Severe epithelial dysplasia n= 19 [Group III]	f-value	p-value
2.35 ±15.62	40.37 ±6.42	43.14 ±4.04	47.67 ±3.31	29.42	0.001

**Table 5:** Comparison of Grades of OSCC with normal mucosa.

Control group n=13 [Group VI]	Well Differentiated n=30 [Group IV]	Moderately & Poorly Differentiated n=20 [Group V]	f-value	p-value
2.35 ±15.62	75.74 ±19.62	92.32 ±15.67	48.71	0.001

stained cells among the total number of cells. The results were tabulated and subjected to statistical analysis including Student's t-test, Chi-square test and Mann-Whitney U-test. The comparisons showed overexpression with increasing grades of Oral Epithelial Dysplasia (OED) and in cases of Oral Squamous Cell Carcinoma (OSCC). Ki-67 overexpression was seen increasing from Grade I to Grade III [Figure 1, 2 & 3]. *p*-value was significant [Table 4]. Similarly, comparisons amongst Group IV and Group V [Figure 4] too showed increase in the mean

value of Ki-67 positive cells. *p*-value was significant [Table 5]. Finally a comparison was done between OED and OSCC which showed increased value in OSCC. These results were significant (*p*-value<0.05).

**Figure 1:** Mild epithelial dysplasia IHC (OL).**Figure 2:** Moderate epithelial dysplasia IHC (OL).

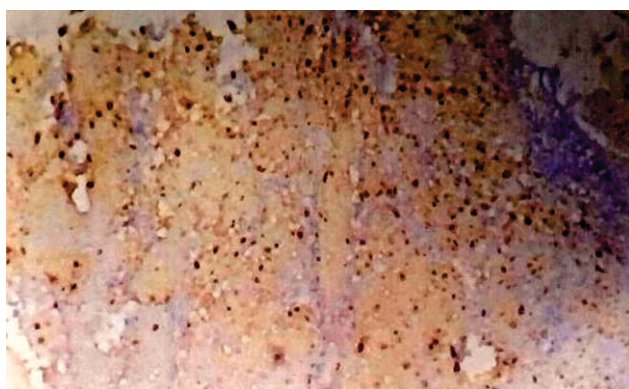
## DISCUSSION:

The ability to reliably predict cancer outcomes can significantly impact the management and biological behavior of lesions, aiming to achieve optimal results in terms of loco-regional control, overall survival, and quality of life. It is well-established that oral lesions (OLs) exhibiting a





**Figure 3:** Severe epithelial dysplasia IHC (OL).



**Figure 4:** Poorly Differentiated squamous cell carcinoma IHC.

histologically moderate to severe degree of epithelial dysplasia have a higher propensity for malignant transformation<sup>[17,18]</sup>. H&E staining is used to routinely diagnose dysplasias. However, the assessment of epithelial changes in the oral mucosa has recognized limitations, representing a significant constraint in predicting the behavior of suspicious lesions. These limitations arise from several factors such as Subjectivity in Histopathological Evaluation, Sampling Errors, Biological Diversity of Lesions, Lack of Molecular Insights.

The study of cellular proliferation markers such as PCNA and Ki-67 continues to be a vital aspect of understanding disease pathology, particularly in oncology. Their role in the diagnostic, prognostic, and therapeutic landscape makes them indispensable tools in modern medicine. Ongoing research and technological advancements promise to further refine their utility and application in clinical practice<sup>[19]</sup>.

Epithelial dysplasia refers to the presence of abnormal cells within the epithelial tissue, indicative of an early step toward potential malignant transformation. This condition is marked by various cellular and tissue alterations, including disrupted cell

maturation and increased suprabasal proliferative activity. Monitoring these changes in potentially malignant disorders (PMDs) can provide crucial insights into the risk of malignant transformation, particularly in tissues like the oral mucosa, cervix, and other epithelial surfaces. Epithelial dysplasia, marked by alterations in cell maturation and increased proliferative activity, is a critical factor in the progression of PMDs toward malignancy. Proliferative markers like PCNA and Ki-67 provide valuable information about the biological behavior of dysplastic lesions, enabling early detection and intervention, ultimately improving patient outcomes<sup>[20]</sup>.

Cell proliferation markers are vital tools in understanding the dynamics of cell growth, especially in the context of diseases like cancer. These markers can be broadly categorized into three types: growth fraction markers, markers of specific cell cycle phases, and cell cycle time markers.

## Categories of Cell Proliferation Markers:

### 1. Growth Fraction Markers:

- These markers indicate the proportion of cells actively engaged in the cell cycle (G1, S, G2, and M phases) as opposed to resting (G0 phase).
- **Ki-67:**

- Ki-67 is a well-established growth fraction marker, present in all active phases of the cell cycle (G1, S, G2, and M) but absent in the G0 phase.
- The intensity of Ki-67 staining and the number of positive cells is generally lower compared to PCNA. This is because Ki-67 is rapidly degraded after mitosis (M phase), whereas PCNA accumulates in cells.
- The monoclonal antibody for Ki-67 detects a nuclear antigen associated with a nuclear non-histone protein, making Ki-67 a reliable indicator of cellular proliferation.

### 2. Markers of Specific Cell Cycle Phases:

- These markers are used to identify cells in particular phases of the cell cycle, providing detailed information about cell cycle dynamics.
- **Examples:**
  - **Cyclins:** Different cyclins are expressed at various phases of the cell cycle (e.g., Cyclin D for G1 phase, Cyclin A for S phase, Cyclin B for G2/M phases).
  - **Phosphorylated Histone H3:** This marker is specifically associated with cells in the late G2 and M phases.

### 3. Cell Cycle Time Markers:

- These markers measure the duration of specific phases or the entire cell cycle, helping to understand the timing and rate of cell proliferation.
- **Bromodeoxyuridine (BrdU):**
  - BrdU is incorporated into newly synthesized DNA during the S phase, allowing researchers to measure the length of the S phase and overall cell cycle time.
  - Detection is usually performed through immunohistochemistry or flow cytometry.

### Ki-67 vs. PCNA

#### • Ki-67:

- Present in all active phases of the cell cycle (G1, S, G2, and M), but not in G0.
- Rapidly degraded after the M phase, leading to lower staining intensity and fewer positive cells compared to PCNA.
- Reacts with a nuclear non-histone protein, which is essential for reliable detection of proliferating cells.
- Considered one of the most reliable markers for cellular proliferation due to its specific expression pattern.

This antigen is present in the nucleoli in G1 followed by nucleoplasmic distribution in later cycle with intensity increasing in S and G2 and being maximum during mitosis<sup>[21,22]</sup>.

Ki-67 was introduced as a potential marker for proliferating cells goes to Johannes Gerdes et al in 1983. The word Ki is derived from the University of Kiel, where Johannes Gerdes in the laboratory of Herald Stein generated antibody. It was the 67<sup>th</sup> well of a 96-well microtitre plate and hence it was designated as Ki-67. After cloning and sequencing the gene, new antibodies were generated and they were named after the division at (M)olecular (I)mmunology (B)orstel. Ki-67 gene is located on human chromosome 10 (10q25)<sup>[23]</sup>.

We Examined 72 cases of OL and 50 cases of OSCC and 13 cases of normal oral mucosa. Out of these, 93% (n=126) were smokers. Affected males were 90.27% in OL and 90% in OSCC.

We used monoclonal antibody Mib-1 was used on paraffin embedded tissue sections to quantify the Ki-67 expression in the epithelium of OL and OSCC. We compared OED with OSCC. In the context of normal mucosal epithelium, the distribution and expression levels of Ki-67 are typically minimal and

predominantly restricted to the basal and parabasal layers. This specific localization reflects the normal proliferative activity of these layers, which are responsible for generating new cells to replace those shed from the surface. The expression of Ki-67 tends to become more pronounced and extensive as the severity of dysplasia increases, progressing from mild to moderate to severe. This trend reflects the increasing proliferative activity and loss of normal cellular regulation associated with higher grades of dysplasia. We found out that, the positivity even extended in the spinous cell layer in severe and some moderate OED. In our study, we found out that the peripeheral cells of the tumor islands showed more positivity compared to the inner cells in OSCC.

Our results were in accordance with other studies<sup>[14,24,25]</sup>. Ki-67 positivity was more pronounced with increasing grades. The results were significant. OSCC compared with OED too showed higher positivity. Suwasini S et al found that Ki-67 overexpression is directly proportional to metastasis to head and neck lymph nodes<sup>[20]</sup>. Similar results were also seen in various other studies<sup>[26,27]</sup>. There have been contradictory results regarding prognosis of OSCC and Ki-67 overexpression. Xie S et al, found that over-expression of Ki-67 in OSCC relates to poor prognosis although suitable treatment timely provided could improve the prognosis<sup>[28]</sup>.

Gonzalez-Moles MA found that ki-67 was over expressed in well differentiated OSCC when compared with poorly differentiated OSCC and hence Ki-67 may not be a reliable prognostic marker<sup>[29]</sup>. The exact reason may be unclear but this may be again due to inadequate sample size.

Ki-67 is a very important and reliable tool for diagnosis and prognosis and has various advantages like simplicity and interpretation of results. Pharmacological modulators of cell proliferation and differentiation have been postulated as the future of cancer preventive drugs. Some of these agents like dimethylfluronithine and retinoids have already been used in clinical trials of OL. Thus the use of Ki-67 could be of great value in montoring the effects of these agents during the course of future chemoprevention trials.

### CONCLUSION:

We conclude that Ki-67 is a reliable marker to predict future outcome of OED and OSCC. It can be used routinely to monitor its progression and treatment modalities.



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Nil.

# Conflicts of interest

There are no conflicts of interest.

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## Research Article

# Morphological Variants of Soft Palate in Patients with Malocclusion – A Digital Cephalometric Research Study

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### ABSTRACT:

**Background-** Patients with cleft lip and palate, swollen adenoids, snoring, poorly retained maxillary dentures, obstructive sleep apnea syndrome (OSAS), and skeletal craniofacial malocclusion are commonly associated with soft palate dysfunctions. We carried out a study in our institute to assess various shapes of soft palate in different malocclusions by Lateral cephalometry.

**Materials & Methods-** 100 OPD patients who came to the department of Oral Medicine and Radiology in our institute formed the study group. The patients were subjected for LC radiograph using Planmeca Proline XC LC along with software Planmeca Romexis 2.9.2.R with Exposure time – 17 sec, mA- 5, kVp- depending on physical status of patient. Radiographs were observed by two experienced oral radiologists at different time period to avoid bias. The soft palate morphology was observed and categorized into six types as suggested by You et al.

**Results-** Out of a total of 100 participants, 57 were classified as Class I, 39 as Class II, and 4 as Class III when malocclusion was examined. 48% had leaf-shaped palates, whereas 35% had rat-tail-shaped palates. Leaf shaped soft palate was most prevalent in males & females. Leaf shaped palate was evident in Class I and Class II, and Butt shaped soft palate was evident in Class III.

**Conclusion-** The comparison of the age, VL, VW and PD of soft plate among different genders, was done. It was found that VL, VW differed significantly. Malocclusion and malocclusion shape, have a strong positive association, based on Pearson correlation test.

**KEY WORDS:** LC, soft palate shape, malocclusion, velar width, velar length.

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### INTRODUCTION:

The soft palate is a fibrovascular portion, and is joined to the back border of the hard palate. It keeps the nasal and oral cavities separate during deglutition and speaking. It takes part in the majority of oral cavity activities, including speech, breathing, and deglutition etc. The soft palate is a moveable flap that rests from the hard palate's posterior edge and slopes back and down between the pharynx's nasal and oral regions. Soft palate is a thick fold of mucosa enclosing an

aponeurosis, muscle tissue, arteries, nerves, lymphoid tissue, and mucus glands.<sup>[1]</sup> Patients with cleft lip and palate, swollen adenoids, snoring, poorly retained maxillary dentures, obstructive sleep apnea syndrome (OSAS), and skeletal craniofacial malocclusion are commonly associated with soft palate dysfunctions.<sup>[2-4]</sup> By analyzing the image of the soft palate on lateral cephalograms (LC), You et al. classified the soft palate into six morphological types (Type 1: Leaf shaped/ lanceolate shaped; Type 2: Rat tail shaped; Type 3: Butt-like shaped; Type 4: Straight line shaped;

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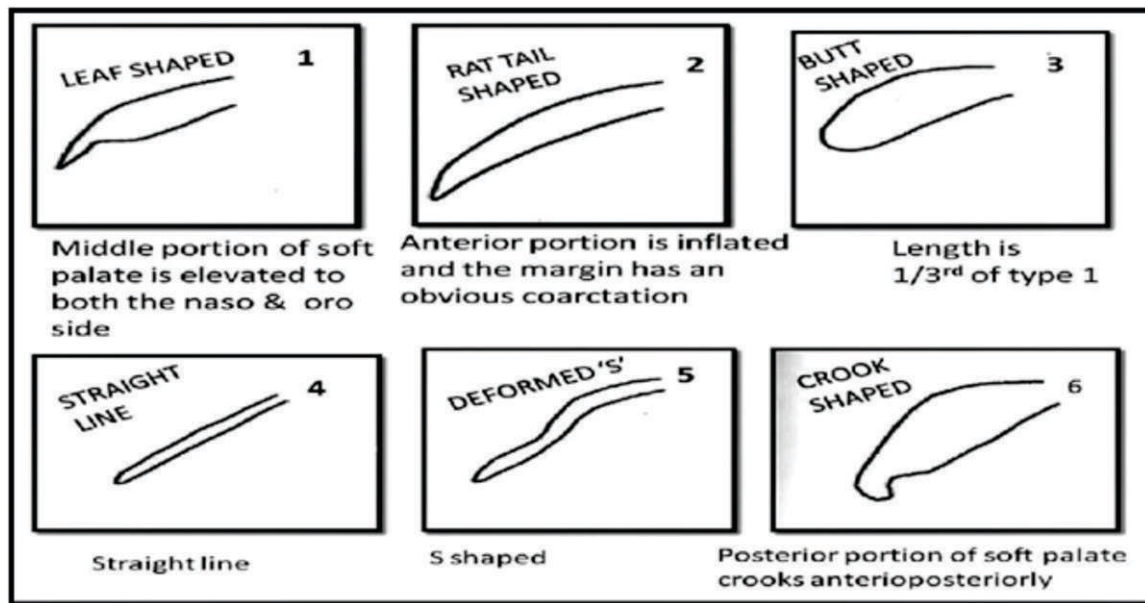
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**Figure 1:** Diagrammatic representation of various shapes of soft palate.

Type 5: S-shaped/distorted soft palate; and Type 6: Crooked shaped)<sup>[2,5,6]</sup> as depicted in Figure 1.

One of the most widely used methods for assessing the six distinct kinds of soft palate that can occur in both healthy persons and in various pathologies is cephalometric examination. LC is economical, more beneficial, simple to do, requires less radiation, and correlates well with other studies like computed tomography. Therefore, it may be used for morphometric assessment of the soft palate and the tissues that surround it.<sup>7</sup> We carried out a study in our institute to assess various shapes of soft palate in different malocclusions by LC.

## MATERIALS & METHODS:

100 OPD patients who came to the department of Oral Medicine and Radiology in our institute, for LC were included in this study. The patients were explained briefly about the study and their consent was taken. Institutional ethical clearance was obtained. They were grouped based on malocclusion. The following inclusion & exclusion criteria was used-

### A) Inclusion criteria:

1. Patients with class I, class II, and class III molar relations.
2. Patient without any syndromes or diseases.
3. Patients within age range of 18-40 years.

### B) Exclusion criteria:

1. Participants with history of trauma, fractures, or surgery.
2. Images with positioning error, magnification, and distortion.

3. Patients who refused to be a part of the study.

The patients were made to sit on a dental chair for clinical examination. The type of malocclusion was evaluated based on Angle's Classification. Thorough intraoral examination was carried out and observations were recorded in a proforma.

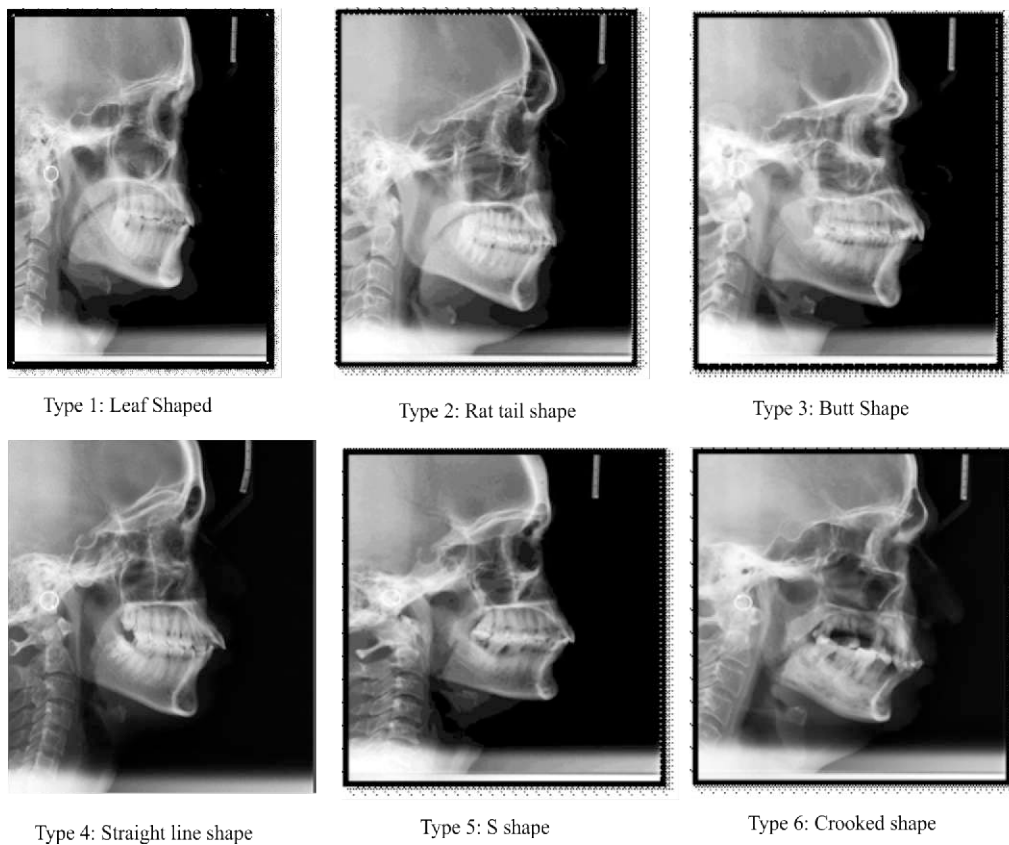
The participants were positioned in cephalostat with Frankfort plane parallel to the floor, and were asked to swallow once to clear any saliva in the oral cavity and pharynx. The participants were then asked to close their mouth tightly to place their upper and lower teeth in centric occlusion with tongue in resting position and relaxed oropharyngeal musculature. The radiographic exposure was obtained by machine using horizontal scanning of the patient.

The patients were subjected for LC radiograph using Planmeca Proline XC LC along with software Planmeca Romexis 2.9.2.R with Exposure time – 17 sec, mA- 5, kVp- depending on physical status of patient. Radiographs were observed by two experienced oral radiologists at different time period to avoid bias. The soft palate morphology was observed and categorized into six types as suggested by You et al (Figure 2).

Linear measurements were carried out, and the length of soft palate was evaluated by measuring the linear distance from the posterior nasal spine to the tip of the uvula of resting soft palate. The width of soft palate along with Pharyngeal depth were recorded from posterior pharyngeal wall to posterior nasal spine.

The velar length (VL) was measured as a linear distance from the posterior nasal spine (PNS) to the tip





**Figure 2:** Types of soft palate observed in the present study.

of the uvula of the resting soft palate [Figure-3 (a)]. The velar width (VW) was taken at thickest section of velum [Figure-3(b)]. The pharyngeal depth (PD) was taken as a linear measurement from the PNS to the anterior pharyngeal wall along the palatal plane [Figure-3(c)]. All these findings were tabulated in an excel sheet. The data was subjected to statistical analysis.

## RESULTS:

The 100 participants in the current study showed that 34 were men and 66 were women. 57 were classified as Class I, 39 as Class II, and 4 as Class III when the malocclusion was examined.

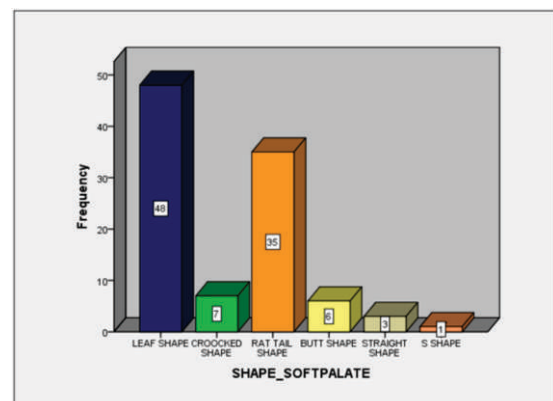
An analysis of the individuals' palate shapes revealed that 48% had leaf-shaped palates, whereas 35% had rat-tail-shaped palates. The palates with the S and straight shapes were least prevalent [Tables 1; Graph 1].

Leaf shaped soft palate was most prevalent in males (n=14) & females (n=34). This was followed by rat tail shape. The results were non-significant [Table 2; Graph 2].

The distribution of various shapes of soft palate among different malocclusions were analyzed and summarized. It was found that leaf shaped palate

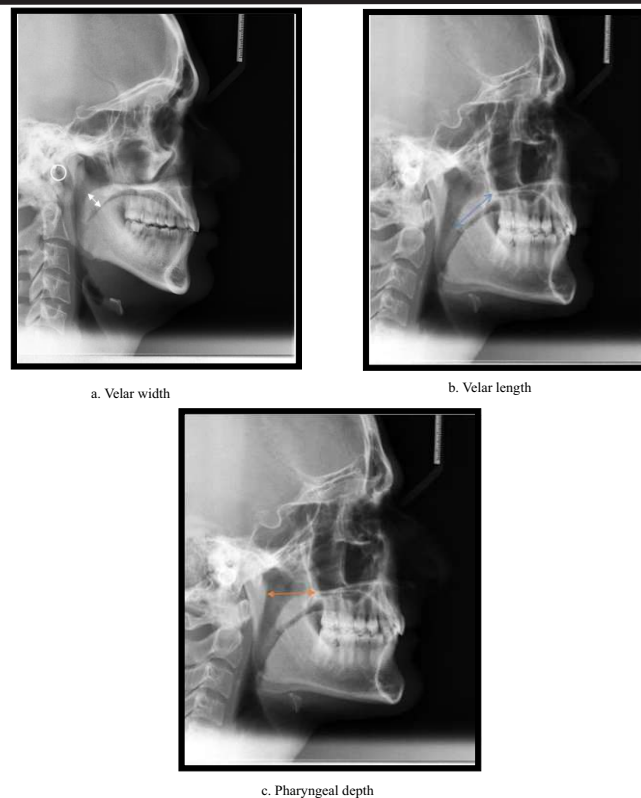
**Table 1:** Descriptive Statistics of shape of soft palate among study participants.

Shape Of Soft Palate	Frequency	Percentage
Leaf Shape	48	48.0
Crooked Shape	7	7.0
Rat Tail Shape	35	35.0
Butt Shape	6	6.0
Straight Shape	3	3.0
S Shape	1	1.0
Total	100	100.0



**Graph 1:** Graphical representation of shape of soft palate among study participants

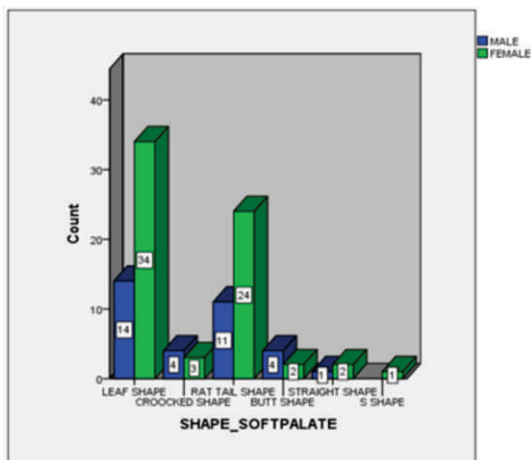




**Figure 3:** 3(a) (VL) Blue line: velar length (Antero-posterior distance); 3(b) (VW) White line: velar width (supero inferior width) and 3(c) (PD) Orange line: Pharyngeal depth.

**Table 2:** Comparison of the types of soft palate shapes among different genders.

Shape Of Soft Palate	Gender						<i>p</i> -value
	Male		Female		Total		
	Count	Column N %	Count	Column N %	Count	Column N %	
Leaf Shape	14	41.2%	34	51.5%	48	48.0%	0.825
Crooked Shape	4	11.8%	3	4.5%	7	7.0%	
Rat Tail Shape	11	32.4%	24	36.4%	35	35.0%	
Butt Shape	4	11.8%	2	3.0%	6	6.0%	
Straight Shape	1	2.9%	2	3.0%	3	3.0%	
S Shape	0	0.0%	1	1.5%	1	1.0%	



**Graph 2:** Graphical representation of types of soft palate shapes among different genders

was evident in Class I and Class II, and Butt shaped was evident in Class III [Table 3].

The correlation was analyzed between types of malocclusion and soft palate shapes using Pearson correlation. It was found that they were significantly correlated with *p*-value less than 0.05 [Table 4; Graph 3].

## DISCUSSION:

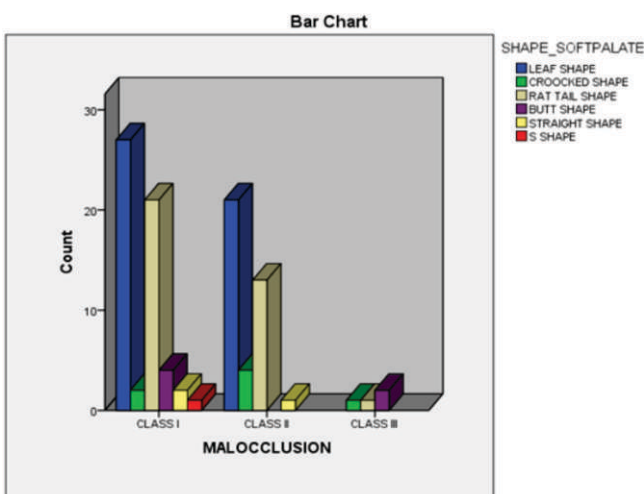
The dimensional analysis of the soft palate and its surrounding structures, especially the VL and VW, has been studied by many investigators. Acquiring careful understanding concerned to the changes noticed in soft palate in different pathologies such as oral submucous fibrosis will be helpful to halt the progression of the disease at that particular stage to

**Table 3:** Distribution of the types of soft palate shapes among various malocclusions

Malocclusion		Count	Percentage	
Class I	Shape of Soft palate	Leaf Shape	27	47.4%
		Croocked Shape	2	3.5%
		Rat Tail Shape	21	36.8%
		Butt Shape	4	7.0%
		Straight Shape	2	3.5%
		S Shape	1	1.8%
Class II	Shape of Soft palate	Leaf Shape	21	53.8%
		Croocked Shape	4	10.3%
		Rat Tail Shape	13	33.3%
		Butt Shape	0	0.0%
		Straight Shape	1	2.6%
		S Shape	0	0.0%
Class III	Shape of Soft palate	Leaf Shape	0	0.0%
		Croocked Shape	1	25.0%
		Rat Tail Shape	1	25.0%
		Butt Shape	2	50.0%
		Straight Shape	0	0.0%
		S Shape	0	0.0%

**Table 4:** Correlation of the types of malocclusion and soft palate shapes

Malocclusion	SHAPE_SOFTPALATE						Total	p-value
	Leaf Shape	Crooked Shape	Rat Tail Shape	Butt Shape	Straight Shape	S Shape		
<b>CLASS I</b>	27	2	21	4	2	1	57	0.014*
<b>CLASS II</b>	21	4	13	0	1	0	39	
<b>CLASS III</b>	0	1	1	2	0	0	4	
	48	7	35	6	3	1	100	

**Graph 3 :** Correlation of the types of malocclusion and soft palate shapes

prevent further complication and restore structural and functional outcomes.<sup>[8]</sup> The study of soft palate patterns like shape, length, width and pharyngeal depth helps for the evaluation of any risk factors for velopharyngeal incompetence. The clinical observation of soft palate is difficult. LC can be used to get an accurate diagnostic. It is relatively inexpensive and aids in the assessment of soft palate morphology and its surrounding structures.<sup>[9]</sup> Advanced diagnostic imaging techniques such as magnetic resonance imaging and fluoroscopy are now available worldwide for imaging of soft palate, but still, LC is preferred imaging technique for the analysis of soft palate for its indispensable advantages. LC is preferred due to its easy accessibility, economical, and relatively good assessment of soft tissue.

In the present study, out of 100 participants, 34 were male and 66 were female. When the malocclusion was checked among all the participants 57 were Class I, 39 were Class II, and 4 were class III. When the shape of palate was analyzed, it was found that most of the participants showed leaf shaped palate (48%), followed by Rat tail shaped palate (35%). The least common was S shaped and the Straight shaped palate.

The comparison of the age, VL, VW and PD of soft plate among different genders, was done. It was found that VL, VW differed significantly, [ $p < 0.001$ ].

On comparing different malocclusions among genders, it was found that they varied significantly [ $p < 0.001$ ]. Different shapes of soft palates were compared among different genders, and it was found that there was no significant difference [ $p > 0.05$ ].

The distribution of various shapes of soft palate among different malocclusions were analyzed and summarized. It was found that leaf shaped palate was evident in Class I and Class II, and Butt shaped soft palate was evident in Class III.

The correlation was analyzed between types of malocclusion and soft palate shapes using pearson correlation. It was found that they were significantly correlated with  $p$ -value less than 0.05.

The majority of the participants showed leaf shaped palate, followed by Rat tail shaped palate. The prevalence of the remaining shapes are as follows Crooked shape (7%), Butt shape (6%), Straight shape (3%), and S shape (1%). The least common was S shaped and the Straight shaped palate.

The results of the current study were in accordance with the study conducted by Ravi prakash et al (2014)<sup>[10]</sup>, where leaf shaped palate followed by Rat tail shaped were most commonly seen. In contrast, the study conducted by Raja Lakshmi et al in 2016<sup>[11]</sup>, the most common shape was found to be butt and crook shape. The least common shape in this study was S shaped and absence of straight line shape (0%) soft palate. This was contrary to Raja Lakshmi et al(2016) study, which showed least common as type 4 and absence of type 5 soft palate.<sup>[11]</sup> These variations could be attributed to smaller sample size in each of the stages of OSMF, whereas in other studies there was no such equal distribution. Another reason could be geographical variations.

The S-shape, which was described as a hooked appearance of the soft palate by Pepin et al in 1999<sup>[12]</sup> was found in 8.3% cases in our study group. Hooking of the soft palate was defined in their study as an angulation of about 30° between the distal part of the uvula and the longitudinal axis of the soft palate. They hypothesized that soft palate hooking plays a key role

in pharyngeal collapse, since hooking results in a sudden and major reduction in the oropharyngeal dimensions, which therefore dramatically increases the upper airway resistance and the transpharyngeal pressure gradient.

In the present study, it was found that most common shape of soft palate among the class I and class II participants was leaf shaped and among class III it was Butt shaped. The correlation was analyzed using pearson correlation test and it was found that the malocclusion was significantly correlated with malocclusion. Subramaniam found that leaf shape was most common in Class I malocclusions, rat tail type in Class II malocclusions, and leaf type and crooked type in Class III malocclusions in the sample of skeletal malocclusions<sup>[13]</sup>. Our study's discrepancy in results could be the result of ethnic variance.

By the 12th week of intrauterine life<sup>[14]</sup>, the soft palate has finished developing, and by the 16th–17th week, the muscles have developed.<sup>[15]</sup> Thus, the development of a soft palate occurs during the intrauterine period. Nonetheless, during the pubertal growth surge, the maxilla and mandible's bone development continues. Furthermore, the definitive malocclusion is determined between the ages 16 and 18. Our research revealed a strong relationship between the different forms of soft palate and skeletal malocclusion. Thus, by looking at the form of the soft palate, we may predict the skeletal malocclusion in children at a very young age.

Therefore, in order to prevent speech issues after treatment, the soft palate dimension and its functional link to the surrounding structure should be considered in the diagnostic and treatment planning of various skeletal diseases. As a result, treatment planning that involves expanding the pharynx ought to be taken into account. When employing orthopedic or surgical techniques, that may require maxillary advancement, the clinician should exercise caution.

## CONCLUSION:

Because of its accessibility, affordability, and somewhat accurate assessment of soft tissue, cephalometric analysis is a widely used method for evaluating soft palates. Numerous studies have addressed the dimensional study of the soft palate and the surrounding structures, particularly the velar length and width; nonetheless, the most logical reason for the variations in soft palate dimensions is the variance in velar morphology.

Malocclusion and malocclusion shape, have a strong positive association, based on Pearson correlation test.

Understanding the wide range of velar morphology may be useful in future studies to determine the etiology of OSA and associated illnesses as well as in the effective functional and structural restoration of the soft palate. However, there is no connection between the soft palate pattern and the treatment of various malocclusions.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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## Review Article

# A Systematic Review on the use of Teledentistry in Pediatric Dentistry

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### ABSTRACT:

Delivering oral healthcare to children can be challenging due to anxieties, access limitations, and geographical barriers. Teledentistry, the use of telecommunication technologies for dental care, has emerged as a potential solution. This systematic review evaluates the effectiveness of teledentistry in pediatric dentistry. A comprehensive search of electronic databases, including PubMed, EMBASE, Scopus, and Web of Science, was conducted to identify relevant studies published with no time frame. The validity of teledentistry for oral screening varies with sensitivity and specificity. Studies also reported acceptable agreement between teledentistry and in-person examinations, with Kappa statistics. Teledentistry shows promise as a comparable tool to traditional methods for oral screening in pediatric dentistry. It holds particular value for school-based programs, remote areas, and long-term care facilities, potentially improving access to dental care for children. Further research with robust methodologies is needed to definitively determine the effectiveness of teledentistry across the full spectrum of pediatric dental care.

**KEYWORDS:** teledentistry, pediatric dentistry, anxiety

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### INTRODUCTION:

Great oral well-being includes the capacity to eat, talk, associate, and partake in a solid eating routine and makes a significant commitment to personal satisfaction. Dental sicknesses, generally preventable, are predominant. Dental specialists additionally assume a significant part in treating abnormalities of the teeth and jaws and recognizing oral appearances of foundational sicknesses.<sup>[1]</sup>

In the early long stretches of 2020, Corona virus 2019 (COVID-19) had spread universally and was before long classified as a pandemic by the World Health Organization (WHO).<sup>[2]</sup> It was accepted to have

begun in Wuhan, China, and is brought about by the profoundly contagious novel Covid (2019-nCoV or SARS-CoV-2) causing serious intense respiratory symptoms.<sup>[3]</sup> By the finish of October 2020, the sickness was accepted to have impacted more than 47 million individuals overall and guaranteed no less than 1.2 million lives.<sup>[4]</sup>

Dentistry has been considered as the most defenceless calling to get impacted by the COVID-19 pandemic, as it includes close investigation, assessment, analysis, and restorative intercessions around the naso-oropharyngeal locale.<sup>[5]</sup> This immensely forceful novel Covid SARS CoV-2, whose

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focal point was Hubei territory in China, was proclaimed as a well-being crisis of worldwide worry by the World Health Organization (WHO) on January 30, 2020.<sup>[6]</sup>

Teledentistry has been characterized by Cook in 1997 as "the act of utilizing video-conferencing innovations to analyze and exhortation about treatment over a distance".<sup>[7]</sup> Teledentistry, a type of telehealth containing a synergism among broadcast communications and dentistry that includes the trading of clinical determined data and important pictures for interview and treatment arranging. The idea has demonstrated to be a help for the ceaseless conveyance of essential medical care administrations during tough spots of the pandemic.<sup>[8]</sup> Innovations as portable applications and other specialized improvements have facilitated the learning and reference convention important to limit direct contact among patients and specialists.

Teledentistry can be advantageous in oral well-being schooling and advancement among kids, analysis and checking pediatric dental patients over significant distances with restricted admittance to dental consideration and in conduct direction of pediatric patients. This technique can be especially valuable during the ongoing pandemic circumstance to restrict patient-to-patient contact by keeping a protected separation. Simultaneously, it forestalls openness of dental staff, dental specialists using cell phones, webcams, intraoral camera and dental applications associated through web.<sup>[9]</sup>

#### ADVANTAGES & DISADVANTAGES:

The Advantages & Disadvantages of Teledentistry are depicted in [Table 1]:

**Table 1:**

S. No	Advantages	Disadvantages
1	Admittance to care for under-served and undertreated population	Treatment requires a visit to the clinic
2	Cost-effective	Technique sensitive and time-consuming
3	Less time consuming	Initial investment
4	Boosted communication	Decreased accuracy
5	Timely diagnosis	Legal issues
6	E-prescription	Language barrier
7	Service in training dental employees at the remote site	Treatment Requires Visits to the Clinic
8	Storing of data	Virtual Examination
9	Management of Preliminary Emergencies	
10	Aiding in Specialist Consultations	
11	Follow-Up Visits Can Be Avoided	

#### TELEDENTISTRY IN PEDIATRIC DENTISTRY:

Teledentistry can be valuable in oral well-being training and advancement among kids, observing pediatric dental patients over significant distances with restricted admittance to dental consideration and in conduct direction of pediatric patients. This strategy can be especially valuable during the ongoing pandemic circumstance to restrict patient-to-patient contact by keeping a protected separation. Simultaneously, it forestalls openness of dental staff, dental specialists using cell phones, webcams, intraoral camera and dental applications associated through web.

The most widely recognized pediatric dental crises incorporate dental torment, dentoalveolar sore, and dental injury. These circumstances require quick intercession as the treatment for these cannot be postponed. Notwithstanding, during the hours of the COVID-19 lockdown, certain adjustments in the underlying treatment were fundamental. Dental agony, endodontic diseases can cause serious torment and are viewed as a significant classification of dental crises. The dental specialist ought to get some information about the idea of agony and assess the condition based on quiet's set of experiences. In the wake of endorsing a reasonable anti-infection course, the dental specialist keeps a legitimate development of the patient. Assuming that the agony reduced, the treatment of the patient could be deferred till the lockdown was lifted. In the event that the aggravation actually did not subside, then, at that point, the dental specialist could call the patient to the center for the crisis treatment. This choice ought to be made by dental specialist in light of the seriousness of the circumstance and his clinical discernment.

Few studies using mobile apps for oral health education and promoting among children are enlisted below  
[10,11,12,13,14,15,16]

Author name and year	Name of the Application used	Purpose of application	Methods	Conclusion
Soler et al., 2009	Molarropolis app	An interactive motivational game aimed at increasing oral health and dental hygiene literacy among adolescents employing persuasion tactics. During the game, players learn about oral diseases and their causes, behaviours and practices that put adolescents at risk, tips on how to improve their oral health.	Survey of individuals aged 13-24 years was done to check the effectiveness of the app in improving awareness and change in habits related to oral hygiene.	Adolescents indicated that the game is both entertaining and informative, helpful to learn new aspects regarding oral health, and has the potential to change oral health habits.
Levine et al., 2012	My Smile Buddy	1. Diet recalls function. 2. Assess risk of early childhood caries due to diet in young children.	Pilot study on mothers (age range not specified) of children with early childhood caries was conducted after training community health care workers (CHW). CHW facilitated use of the app by the mothers. Survey of CHW for ease of navigation and usefulness of the app.	Community Health care Workers rated the app as very easy and fun for the families to use.
Shao et al., 2014	DAYA tooth brushing game	A tooth-brushing game to enhance the efficacy and experience of tooth brushing in children, and helping the parents to monitor child's dental health and behaviour towards oral hygiene.	A pilot study involving 6-10-year-olds on usability testing of the mobile application and the game.	The game was better understood by older children (>8 years of age) and found them enjoyable. Parents were able to complete all the tasks related to monitoring. The game was feasible in enhancing the tooth brushing experience for children and monitoring by parents.
Underwood et al., 2015	Brush DJ app	1. Provide users evidence-based routines to maintain oral hygiene. 2. Motivation by playing music for 2 min while brushing. 3. Set reminders for rinsing mouth, maintain concentration of fluoride, frequency to change toothbrush, dental appointment schedule.	Qualitative survey assessed perception regarding experiences and beliefs regarding oral health app amongst participants aged up to 74 years of age. Majority of the participants (37.1%) were in the 7-12 year age group.	Mobile app is useful for oral hygiene education and promotion. It motivated the participants to brush for longer time. The themes were motivation, education, compliance and perceived benefits.
Alqarani et al., 2018	Your child's smile	Provide information to parents regarding oral health of their child pre-partum and from the period of infancy to adolescence. Format of both apps were same.	Survey to assess improvement in parent's knowledge before and after the use of the mobile app in children up to 15 years of age.	Significant improvement in knowledge related to dental caries and oral hygiene.
Zotti et al., 2019	1. Time2Brush (Children >5 years). 2. Little Monsters Toothbrush time (Children 5 years).	Fictional characters served as motivation to practice oral hygiene along with a stopwatch to perform routine procedures. Additionally, according to the minutes of use, users could customize the summary accordingly, as a bonus.	Randomized trial involving study and control group involving 4-7-year-old children. Chair side instructions on oral hygiene for control group.	Decrease in plaque scores, no new caries lesions on permanent molars. Better compliance for oral hygiene by children, increase in knowledge level of parents.
Alkilzy et al., 2019	Manual toothbrush with sensor that is linked to the smart phone via Bluetooth	Manual tooth brush with a digital motion 3D sensor system (gyroscope), so that the tooth brush follows the tooth brushing movements of the child in real-time. The movements are relayed to smart phone via Bluetooth. Movements are shared with parents for monitoring and as the child reaches optimal movements points are awarded.	A randomised control study evaluating effectiveness of using a manual toothbrush with a gravity sensor and used along with a mobile tooth brushing app in children aged 5-6 years. The control group used a manual tooth brush without the smart phone app.	Decline in plaque index was more pronounced in the test group than in the control group, which gives evidence for the effectiveness of gaming in toothbrushing via a smart phone app.

The following studies using social networking media for oral health education and promoting among children are enlisted below <sup>[17,18,19,20]</sup>:

Author name and year	Name of the media used	Purpose of application	Methods	Conclusion
Zotti et al., 2016	WhatsApp	Video tutorials regarding oralHygiene. Self-photographs (selfies )and text messages shared bypatients and their parents viaWhatsApp-based anonymous chatroom .	Randomized controlled trial involvingAdolescent patients (mean age 14.1 years in study group and 13.6 years in control group) undergoing orthodontic treatment requiring maintenance of oral hygiene. Patients and parent were asked to interact via selfies and text messages pre and post oral hygiene practices.	Improved compliance to oral hygiene inpatients noted with lesser white spot lesions recorded during orthodontictreatment.
Scheerman et al., 2019	Telegram	Theory based program consistingof oral health education andbehaviour coaching components topromote regular tooth brushing.	Randomized controlled trial evaluatedeffectiveness of Telegram application inpromotion of oral hygiene and oral health related outcomes in adolescents aged 12-17-years along with mothers. Theoutcomeswere based on improvements intooth brushing behaviour and –plaque scores.	Results supported use of health actionprocess-basedapproach and theory -based program through Telegram with involvement of mothers to improve oral hygiene among adolescents.
Lotto et al., 2020	WhatsApp	Educational text messages relatedto early childhood caries.	Randomized controlled trial including child-parent dyad with in children aged 36 to 60 months and having early childhood caries. The intervention groupreceivedEducational WhatsApp text messages.	Effective to control the severity of ECC in low socioeconomic pre-schoolers,improving parental eHealth literacy andChanging children's dietary patterns.
Simsek et al., 2020	YouTube	YouTube videos describing oralhabits searched	Evaluated videos on oral habits and assessed quality of information available for patients and parents.	Majority was inappropriate withInadequate information.

#### DENTAL ABSCESS OR SWELLING:

The persistent instances of agony or dental contaminations in some cases fuel as a boil or

enlargement. In this condition, the dental specialist can request that the guardians send an extra-oral and intra-oral photo of the kid. This assists the dental specialist

The following studies with telediagnosis using smartphone camera/ digital camera/ web camera in children are enlisted below <sup>[21,22,23,24,25,26,27]</sup>.

Author name and year	Device for diagnosis	Methods	Conclusion
Am_avel et al., 2009	Digital camera, Web-based system( MedQuest)	Validity of the remote diagnosis of dental problems in 4–6-year-old children was done by dentists using digital camera. Screening and referrals were decided based on images obtained via web-based application.	Use of photographs is a valid method for remote diagnosis of dental problems. Specificity of this method of screening can be enhanced by improving feedback on dentist's evaluation.
Torres -Pereira et al., 2012	Smartphone camera	Non-Randomized study wherein intra-oral images of first 60 patients (irrespective of age) who visited the dental clinic after ethics committee approval were uploaded on cloud-based servers by dental assistants for mid-level practitioner's and dentists to screen for dental caries.	Photographs taken with 18-megapixel DSLR were able to provide adequate diagnostic information with sensitivity and specificity. Photographic assessment accelerated referrals to specialists that reduced delayed treatment and increased patient inflow.
Kopycka-Kedzierawski et al., 2013	Intra-oral camera	Randomized comparative evaluation between conventional dental examination and teledentistry aided examination in assessment of early childhood caries prevalence in 12e60-month-olds.	No difference between either type of examination. Provision of coloured pictures of child's cariously exposed teeth helped in motivating parents forgetting their children examined.
Purohit et al., 2017	Smartphone camera	Dentists involved in this cross-sectional survey conducted a clinical versus video-graphic examination to assess DMFT index in 12-year-old children.	Clinical and video-graphic methods of assessment were proven to be comparable for screening of dental caries in school children.
Estai et al., 2017	Remote mobile Teledentistry system for Android phones with 'Remote-i' cloud server that collects, transmits and reviews dental photographs.	Study compared cost-effectiveness of conventional visual-tactile examination with teledentistry approach. Trained tele-assistants carried out dental screening of all age groups, including children, using recorded photographs that were later shared via 'Remote-i' system.	Teledentistry is cost-effective method that can be used for mass dental screening in distant locations.
de Almeida Geraldino et al., 2017	Mobile phone camera	Cross sectional study involving patients between 3-39 years of age with traumatized teeth. Remote Examination by paediatric dentists using electronic records and photographs. Agreement with in surgery and remote diagnosis was evaluated.	Precision of remote diagnosis was comparable to the diagnosis conducted in person. Mobile phone camera can be a useful tool to capture images for remote diagnosis of traumatic dental injuries.
Kale et al., 2019	Smartphone camera, social networking application (WhatsApp)	Mothers' ability to diagnose dental caries in 3- to 5-year-old via smart phone camera post health education was assessed. The captured photographs were shared with dentists via WhatsApp.	The method recorded good sensitivity, specificity and accuracy. Children were more cooperative for Examination with smart phone in comparison to conventional visual examination as they are familiar with the former.



with assessing the degree of the enlarging in a vastly improved manner. In the event that the expansion is intraoral and not broad, a standard anti-infection course can be given to the patient. This generally is adequate for decrease in size of the expanding and mediation can be deferred. In the event that the enlargement is extra-oral and broad, a crisis dental arrangement should be planned.

### DENTAL TRAUMA:

During the hours of the lockdown, most kids would generally play at home. This invigorated the requirement for additional energetic methods of play in youngsters and cause an expanded gamble of dental awful wounds. In the event of an episode of dental injury with negligible draining and aggravation, the use of strain to the draining site and appropriate mitigating medications could be endorsed. In serious cases, for example, separation, confounded crown and root break or injury to the encompassing tissues, crisis mediation is required.

### CONCLUSION:

Teledentistry, the underpinning of which lies in the web and advances in data innovation can be an enhancement to eye-to-eye techniques for pediatric dental consideration, at last prompting better quiet administration. Pediatric dental specialists can use this innovation for patient/parent training, checking preventive consideration and post treatment follow-up, evaluation of dental turn of events, analysis of dental illnesses, treatment arranging and pre-arrangement conduct direction to diminish nervousness among youngster patients. This mechanical progression in dentistry can make a critical commitment in diminishing the hole between the organic market of pediatric dental experts where oral medical services offices are restricted. The utilization of teledentistry during the pandemic extends the capability of this innovation to lessen the spread of infection. Further examination is expected for protected, compelling and proof-based utilization of teledentistry in the field of pediatric dentistry. Notwithstanding the disadvantages, teledentistry can be a device to give long haul oral medical services to the pediatric populace, defeating the imbalances in admittance to expert consideration. This requires shared endeavours by the wellbeing specialists and pediatric dental specialists. With every one of the mechanical advancements occurring in the field of teledentistry, experts may ultimately connect up to virtual dental well-being facilities and an altogether new time of dentistry can be made. The future could likewise see far off telemedical control of robotized

instruments in circumstances with long haul inaccessibility of dental consideration, e.g., during space flights, on overseas ships, and in different rustic regions. The outcomes accomplished so far are exceptionally uplifting, setting the street finishes paperwork for future examinations. Notwithstanding, various things must be addressed before teledentistry can ascend to its pinnacle. Further investigations including more prominent number of members will be expected to approve the different parts of teledental applications.

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### Conflicts of interest

There are no conflicts of interest.

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## Review Article

# Artificial Intelligence-Powered Pediatric Dentistry: A Glimpse into the Future

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### ABSTRACT:

The rapid digitalization of various aspects of life has significantly transformed dentistry, improving the quality of dental care through advanced technologies like artificial intelligence (AI). AI, which replicates human cognitive processes, has revolutionized dental practices by automating time-consuming tasks and offering precise diagnostics and treatment plans. Despite being in early development stages, AI in dentistry signifies a disruptive technology poised to redesign clinical care. Innovations such as CAD/CAM systems, intraoral imaging, and digital radiography illustrate AI's applications in caries diagnosis, implant design, etc. Historical milestones, from conceptualization of AI to advancements in machine learning and neural networks, have paved the way for sophisticated AI models used in various dental specialties, including pediatric dentistry. AI's potential extends to patient education and practice management, promising a future where dentistry is increasingly efficient, accurate, and patient-centered. This review highlights role of AI in pediatric dentistry with special mention of review of literature.

**KEYWORDS:** Artificial Intelligence, Dentistry, Deep Learning, Machine Learning, Neural Networks

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### INTRODUCTION:

As we all know, the world is rapidly moving toward digitalization in all aspects of life. This digital revolution has transformed dentistry in every aspect and increased the quality of dental care. The term "artificial intelligence" (AI) elicits strong feelings. For one thing, there's our fascination with intelligence, which appears to give us a unique place among living beings. Questions such as "What is intelligence?" "How can intelligence be measured?" and "How does the brain work?" arise and all these questions are relevant when trying to understand artificial intelligence.<sup>[1]</sup> AI aims to replicate human cognitive processes and achieve the same results as medical professionals in a much shorter time frame. It excels at

extracting information from historical data and helps doctors by automating time-consuming tasks.<sup>[2]</sup>

Although AI development is still in its early stages, and medical tasks that modern AI can perform can almost be done by humans, the emergence of AI in dentistry signifies a new era of disruptive technology with the potential to completely redesign the landscape in which dental clinical care is practiced.<sup>[3]</sup> Over the years, man has attempted to build technology that can simulate the proper functioning of the human brain, which has resulted in the advancement of technology known as AI.<sup>[4]</sup> The exponential growth of science and technology has resulted in unique applications that are used on a daily basis, such as Siri and Alexa. These programmes are discovered at the peak of AI and its

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components. The term AI is commonly associated with robotics. It describes how technology is used to create software programmes or a system that can easily mimic human intelligence and carry out specific tasks.<sup>[5]</sup>

John McCarthy in 1955 coined the term "artificial intelligence," and he is widely regarded as the father of AI. He chose this term to explain the ability of machines to perform duties that could fall under a variety of "intelligent" activities.<sup>[6]</sup>

CAD/CAM and intraoral imaging—both laboratory and clinician controlled—are examples of how technologies are being used in dentistry. The technologies are used in caries diagnosis, in computer-aided implant dentistry, including the design and fabrication of surgical guides; in digital radiography (intraoral and extraoral), including cone beam computed tomography (CBCT); in electric and surgical/implant handpieces, lasers, occlusion, and temporomandibular joint (TMJ) analysis and diagnosis; in photography (extraoral and intraoral); in practice and patient record management, including digital patient education; and in shade matching.<sup>[7]</sup> With all of these digital dentistry implements assisting dentistry around the world, researchers and inventors are further encouraged to seek out new technologies or advancements that can be used to elevate the profession to its peak.<sup>[8]</sup> In the modern-day world, AI refers to any machine or technology that is able to mimic human cognitive skills like problem solving.<sup>[5]</sup> To understand AI, it is important to know few key aspects as depicted in (Figure1).

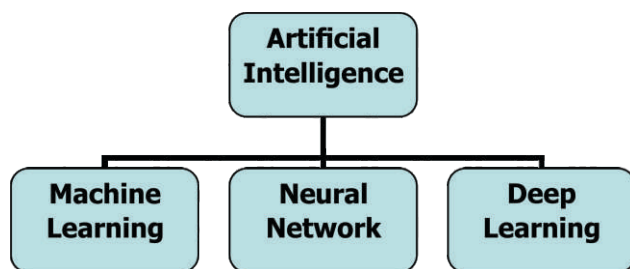


Figure 1: Key aspects of artificial intelligence.

## HISTORY OF ARTIFICIAL INTELLIGENCE:

**HISTORY OF NEURAL NETWORKS:** 1943- Warren McCulloch and Walter Pitts published a paper in which they proposed using neural networks to mimic human brains.<sup>[9]</sup>

1951- The stochastic neural analogue reinforcement calculator developed by Minsky and Dean Edmunds is regarded as the first neural network in history.<sup>[10]</sup>

1955- For the first time in history, Allen Newell and Herbert Simon created AI applications. The Logic

Theorist programme proved 38 of the first fifty-two axioms of Principia Mathematica, a work co-authored by Whitehead and Russell.<sup>[11]</sup>

Although the possibilities for implementing strong AI were unclear, the evolution of weak AI through the creation of artificial neural networks continued. Arthur Samuel extended the development of weak AI in 1959 by coining the term "machine learning."<sup>[12]</sup>

## Development of Deep Learning:

The field of research and development focused on the implementation of weak AI and this trend was accelerated by Arthur Bryson and Yu-Chi Ho.<sup>[13]</sup>

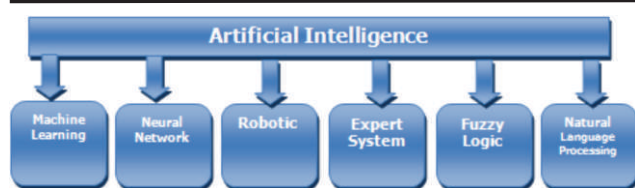
In 1969, they developed the back propagation algorithm. They made a significant contribution to the current implementation of deep learning. This back propagation algorithm refines the AI execution result using a partial derivative approach, which is implemented propositionally and symbolically and is intended to improve the AI-auto-executing algorithm.<sup>[14]</sup> AI advances from the level used for Turing test implementation and mathematical and logical verification to the higher level of real-world usage through the concept of machine learning.

An early expert system emerged in 1972, which is a system that allows non-specialists to apply expertise by organising and processing expert knowledge in a specific field.<sup>[15]</sup>

MYCIN, a 1972 expert system developed at Stanford University, is designed to identify microorganisms that cause serious infections and to recommend appropriate antibiotics.<sup>[16]</sup>

In 1956, Marvin Minsky and John McCarthy (a computer scientist at Stanford) hosted approximately eight-week-long Dartmouth Summer Research Project on Artificial Intelligence (DSRPAI) at Dartmouth College in New Hampshire. This workshop, which kicked off the AI Spring and was funded by the Rockefeller Foundation, brought together people who could be considered the founding fathers of AI. Nathaniel Rochester, the computer scientist who later designed the IBM 701, the first commercial scientific computer, and mathematician Claude Shannon, who founded information theory, were among those who took part. The goal of DSRPAI was to bring together researchers from various fields in order to establish a new research area devoted to developing machines capable of simulating human intelligence.<sup>[17]</sup>

AI is a branch of computer science that aims to understand and build intelligent entities often instantiated as software programs.<sup>[18]</sup> The branches of Artificial intelligence are depicted in Figure 2.



**Figure 2:** Branches of artificial intelligence.

## MACHINE LEARNING:

Machine learning (ML) is a branch of AI in which systems learn to perform intelligent tasks without prior knowledge or hand-crafted rules. Instead, the systems identify patterns in examples from a large data sets, without human assistance.<sup>[18]</sup>

ML has an advantage that newly designed AI model enables the radiologist to develop more and increase their level of learning with a large database of new images. ML depends on algorithms to predict outcome based on data sets.

## DEEPLARNING (DL):

It is sub branch of ML that utilizes the networks with different computational layers in deep neural networks to analyse data. It utilizes varied computational layers through a deep neural network, thus analysing the input data. DL is to generate patterns to improve feature detection. DL structures referred to as convolutional neural networks (CNNs), which can extract many features from abstracted layers of filters, are mainly used for processing large and complex Images.<sup>[19]</sup>

DL is being accelerated by the development of self-learning back-propagation algorithms that progressively refine the results from the data, as well as by increase in computational power. Due to these rapid technological advances, AI, represented by deep learning, can be used for real-life problems, and is applied across all sectors of society.

The diagnostic accuracy of deep learning algorithms in the medical field is approaching levels of human expertise, changing the role of computer-assisted diagnosis from a 'second-opinion' tool to a more collaborative one.

Multiple studies have shown that deep learning algorithms performed at a high level when applied to breast histopathology analysis, skin cancer classification, cardiovascular diseases' risk prediction, and lung cancer detection.<sup>[20]</sup>

## Artificial neural networks:

Artificial Neural Networks were invented keeping the structure of the brain as its basis and it has the ability to imitate human brains.<sup>[5]</sup> In 1951, Minsky

and Dean Edmunds developed the stochastic neural analog reinforcement calculator, which is recognized as the very first neural network in its developmental history.<sup>[6]</sup> In 1955, Allen Newell and Herbert Simon developed programs of AI for the first time.<sup>[12]</sup>

The greatest advantage of these systems is that they have capability to solve the problems that are too complex to be solved by conventional methods. They are useful in various areas of medicinal science like diagnosis of diseases, biomedical identification, image analysis and data analysis. In dental practice also the clinical support systems are actively progressing.<sup>[9]</sup>

## ROLE OF AI IN DENTISTRY:

**Periodontology-**Wang et al. developed a Digital Convolution Neural Network based system that consists of 16 convolution layers and two fully connected layers for detecting periodontitis of premolars and molars.<sup>[21]</sup>

DL analysis using radiographs can help in diagnosis and treatment planning of periodontal diseases by the early detection of periodontal changes. This helps in early intervention in implantology. In addition to promoting our understanding of periodontitis, this technology serves as a bridge to incorporate conventional indicators and immunologic and microbiological parameters into periodontal diagnosis.<sup>[18]</sup>

AI is being used in pediatric dentistry and periodontology to detect dental plaque and diagnose gingivitis and periodontal disease using intraoral photographs and fluorescent images. AI models have been used to detect plaque on primary and permanent teeth, predict children's oral health status and treatment needs, detect, classify, and predict dental caries, detect and categorize fissure sealants, determine chronological age, and determine the impact of oral health on adolescent quality of life. Table 1 shows findings of studies that used AI in periodontics.<sup>[22,23,24,25]</sup>

## Endodontics:

In terms of detection, determination, and disease prediction in endodontics, AI has shown accuracy and precision. In order to increase the success of endodontic treatment outcomes, AI can help to improve diagnosis and treatment.

## Oral Radiology:

In the fields of medicine and dentistry, many AI models have been produced to assess people's risk of getting sick, detect abnormal health data, diagnose and prognosis of diseases. Since digital images are used for

**Table 1:** AI in periodontics.

Author	Year of Publication	Algorithm Architecture	Objective of the study	Conclusion
K. Carter et al.	2004	Automated quantification	To assess the accumulation of plaque on teeth, a fully automated method was developed based on digital imaging of methylene blue (1% w/v) disclosed plaque.	This method has potential for automated and quantitative measurement screening of dental plaque that may be used to assess the efficacy of oral hygiene products and procedures.
J. Kang et al.	2006	Cellular Neural Network	This paper presented an approach for quantifying the dental plaque automatically based on cellular neural network (CNN) associated with histogram analysis.	The experimental results showed that this method provided accurate quantitative measurement of dental plaque compared with that of traditional manual measurement indices of the dental plaque.
Imangaliyev et al.	2017	CNN	An image classification model based on Convolutional Neural Network is applied to Quantitative Light-induced Fluorescence images.	The model directly benefits from multi-channel representation of the images resulting in improved performance when, besides the Red colour channel, additional Green and Blue colour channels are used.
You et al.	2020	CNN	To design a deep learning-based artificial intelligence (AI) model to detect plaque on primary teeth and to evaluate the diagnostic accuracy of the model.	AI model showed clinically acceptable performance in detecting dental plaque on primary teeth compared with an experienced pediatric dentist. This finding illustrates the potential of such AI technology to help improve pediatric oral health.

**Table 2:** AI in endodontics and oral radiology.

Author and year\	Study design	Year of publication	Algorithm Architecture	Objective of the study	Conclusion
Saghiri et al.	Experimental	2012	ANNs	ANN based AI model for determining the working length	The accuracy of ANN was more than the endodontists
Campo et al.		2015	BNNs	Bayesian networks for predicting the need for performing a retreatment	The proposed system with Bayesian networks was tested in a real environment and the results obtained are promising.
Hatvani et al		2018	CNNs	To investigate the use of CNNs for Resolution enhancement of 2-D CBCT dental images, using CT data of the same teeth as ground truth	The results suggest the superiority of the proposed CNN based approaches over reconstruction based methods
Ekert et al.		2019	CNNs	CNNs for detecting apical lesions (ALs) on panoramic dental radiographs To evaluate the use of convolutional	A moderately deep CNN showed satisfying Discriminatory ability to detect ALs on panoramic radiographs
Fukuda et al		2020	CNNs	Neural network (CNN) system for detecting vertical root fracture (VRF) on panoramic radiography CNNs to detect	The CNN learning model has shown promising results in detecting VRFs on panoramic images
Orhan et al.		2020	CNNs	periapical pathosis on cone-beam computed tomography (CBCT) images	The performance of humans and by AI systems were comparable to each other



diagnosis in the field of radiology, it is quite easy to transfer these digital data into computer language. Thus, radiology is the most suitable branch of dentistry for AI use. Table 2 shows findings of studies that used AI in endodontics and oral radiology.<sup>[26,27,28,29,30,31]</sup>

### **AI IN PEDIATRIC DENTISTRY:**

In Pediatric dentistry, AI has many potential applications which would change the face of behavioural Pediatric practice in future. Also, with the help of larger data sets, ML algorithms will only become more sophisticated over time.

AI is also gaining pace in the early orthodontic tooth movement with customized AI driven appliances which would have better acceptability by the new generation. AI enabled restorative dentistry with computer-aided design computer-aided manufacturing technology is already established in adult dental practice and would emerge a boon to pediatric restorations in terms of time and aesthetics. Pain control with AI enabled devices is the new, smarter way towards injection-free pedodontic practice.

Also, AI can be used to enhance the teaching and learning process for students as well as patients. The various 4D goggles, movies, animations and virtual reality-based games can be used as a behaviour modification aid effectively for Pediatric patients. Thus, a dramatic improvisation of AI based Pediatric dentistry would change the way we practice as well as teach. Dentistry and oral healthcare, promisingly, is a very natural customer for artificial intelligence applications in the near future.<sup>[32]</sup>

Early childhood caries (ECC) is a multifactorial disease with host, microorganisms, diet, and oral hygiene practices as the factors that determine the risks. Children's parents/caregivers need to be engaged around these risk factors and acquire skills to self-manage risk to reduce children's risk for ECC.

To combat this ECC pandemic and overcome the barriers of lacking dental access among underserved children and lacking self-management awareness of these children's caregivers, our long-term goal is to develop a first-of-its-kind AI-powered smart phone app to be used by children's parents, which offers patient-centered caries detection and caries risk management.

### **FUTURE OF AI IN PEDIATRIC DENTISTRY:**

AI has many potential applications in paediatric dentistry that will change the face of behavioural paediatric practise in the future. Furthermore, as larger data sets become available,

machine learning algorithms will only become more sophisticated over time. The new, smarter approach toward pedodontic practice without injections is pain control with AI-enabled devices. AI can also be used to improve patient care and teaching and learning processes for students. Children patients can benefit greatly from the various 4D goggles, films, animations, and virtual reality-based games as a tool for behaviour modification. As a result, a radical improvisation of AI-based pediatric dentistry would alter both our practice and our teaching methods. A promising market for AI applications in the near future is dentistry and oral healthcare.<sup>[33]</sup>

### **INNOVATIONS THAT CAN TRANSFORM DENTISTRY IN FUTURE:**

**Use of Software in Dentistry-** Currently, softwares are used by dentists to gain insights on clinical decision-making. To help physicians choose the optimum modalities for their patients, these will grow further to incorporate AI algorithms. Dental medicine is moving towards a new phase of digitization as a result of the exponential growth in clinical information and the development of healthcare AI. These clever algorithms can be incorporated into the healthcare system to analyse patient information, scientific discoveries, and therapeutic approaches to provide diagnostic and therapeutic recommendations.

#### **Use of Tooth Brushes with Brain:**

An intelligent electric toothbrush ensures that you will be brushing your teeth properly and provides children with enjoyable games to maintain the healthy habit of brushing their teeth on a regular basis. The handle of smart toothbrush is jam-packed with sensors. These provide you immediate feedback through a companion app, alerting the user if he/she is using too much force, while brushing.

#### **Designing with Computers & 3D Printing:**

In computer-aided designing (CAD) & computer-aided manufacturing (CAM), 3D printing, is gaining importance. Traditionally, a dentist must create a mould of the patient's tooth and create a temporary crown before waiting for the dental facility to create a permanent one. Using CAD/CAM technology, the tooth is drilled to prepare it for the crown, and a bitmap picture is then taken. Then, a device that receives and sends this image makes the crown in-office.

In fact, 3D printers may be used to make orthodontic models, surgical implants, aligners, retainer, etc more rapidly and precisely. This helps in

streamlining procedures and decreases errors and labor cost, which ultimately increases the technology's efficiency in terms of time and cost.

### ADVANTAGES OF AI:

AI enables Diagnostic and treatment planning efficiency. It can be used for Program standardization. It is faster and takes less time. From a patient's point of view, AI could help overcome the flaws in traditional dental care that have been widely criticized. Dentistry, and specifically dental academia, has a role to play in ensuring that AI improves dental treatment while lowering costs, benefiting patients, treatment providers, and society as a whole. AI in dentistry is emerging as a benefit to clinicians in improving patients and simplifying complicated protocols by providing predictable outcomes.<sup>[16]</sup>

### DISADVANTAGES OF AI:

One of the major disadvantage is that AI's mechanism is quite complicated. Costs of setup are high. Due to the large amount of data required to train and precision, it is challenging to attain accuracy in rare disorders or diseases.<sup>[1]</sup> Ethical issues in the biomedical environment are of concern.<sup>[32]</sup>

### CONCLUSION:

Currently, AI has entered various areas of dentistry and has provided significant services in each of these areas. However, in many areas, there have been interesting but failed efforts and ideas, with further progress being made in using the potentials of AI. Going into the phase of investment in AI projects in pediatric dentistry can lead to facilitation of their deployment and to new developments of efficiency in the field of pediatric dentistry. According to our background review of existing dentistry AI technologies, we assume that different processes in the dental profession are largely multidimensional and require various subtleties in different areas. By looking at the types of subsets of AI and spectating their progress, it seems that AI is at the service of the dentists to augment their intelligence and efficiency, rather than being a threat for employment processes in the dentistry sector.

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There are no conflicts of interest.

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## Case Report

# Ectodermal Dysplasia – A Case Report and Comprehensive Literature Review

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### ABSTRACT:

Ectodermal dysplasia (ED) is a rare genetic condition characterized by a variety of deformities in ectodermal derivatives. Skin, nails, hair, teeth, and exocrine glands are derived from ectodermal germinal layers during the development of an embryo. ED has been reported in more than 150 variants in the literature. An average of seven cases are reported for every 100,000 live births. anhidrotic (Hypohidrotic) and hydrotic ED are the two types based on the degree of function of sweat glands. A 42-year-old male with characteristic features of ectodermal dysplasia visited our dental department and was treated with complete denture prosthesis described in this case report.

**KEYWORDS:** Ectodermal dysplasia, Shamroth-window test, Complete denture.

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### INTRODUCTION:

Ectodermal dysplasia (ED) disorder is a rare inherited disease characterized by primary developmental defects<sup>[1]</sup>. One or more diversified ectodermal structures are affected, including hair, sweat glands, teeth, and nails, eyes, ears, and nervous system<sup>[1]</sup>. It can also affect other endocrine glands of ectodermal origin such as pituitary gland, adrenal gland, and exocrine glands such as meibomian glands, lacrimal glands<sup>[1]</sup>. The incidence of ED is estimated to be around seven cases per 100,000<sup>[2]</sup>. The degree to which sweat glands function determines the type of ED<sup>[2]</sup>. A classical triad of hypohidrosis, hypotrichosis, and hypodontia is exhibited in the first type of X-linked hypohidrotic disease<sup>[3]</sup>. The second variant of ED, the hydrotic type, occurs as an autosomal dominant and exhibits a lack of development and involvement of the

sweat gland<sup>[3]</sup>. There is still no clear understanding of how ectodermal dysplasia occurs or the underlying molecular mechanisms behind or associated with these disorders<sup>[3]</sup>. ED has been linked to loss-of-function variants of the epilepsy-associated repeats, Thrombospondin Type Laminin G Domain And Epilepsy Associated Repeats (TSPEAR) gene<sup>[4]</sup>. The expression of genes that regulate the signaling pathway notch and play a role in murine tooth and hair development was altered as a result of TSPEAR mutations or down-regulation<sup>[5]</sup>. The function of this gene in the human hair follicle and tooth morphogenesis is still unknown, so to evaluate its phenotypic association further functional evidence is needed<sup>[5]</sup>. In this case report, we aim to present concepts on theoretical aspects of our discipline and advise potential solutions for similar cases in the future.

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**CASE PRESENTATION:**

A 42-year-old male presented to our department with a chief complaint of missing teeth. History revealed he was born from parents of consanguineous marriage. He has no teeth from birth. Extraoral examination revealed sparse hairs on the head and complete loss of hair in both eyebrows, frontal bossing, discrete pigmented papules on the forehead skin, periocular pigmentation due to darkening of the skin around the eyes, saddle nose, depressed nasal bridge, increased intercanthal distance, and coarse thick lips [Figure 1].



**Figure 1:** Extraoral clinical examination revealed sparse hair on head, frontal bossing, periocular hyperpigmentation, depressed nasal bridge, coarse thick lips

On further extraoral examination revealed dryness (hypohidrosis) and discrete hyperpigmented papules on forehead skin, sparse hair and severe recession of hairline on head [Figure 2A, B].

On further clinical examination of his lower limbs a flat spoon-shaped nail bed with loss of lustre on his left greater toe of his left leg [Figure 3].

Extraoral examination also revealed convexity of nail plates on all his finger digits and dry pigmented skin on the external surfaces of his hands [Figure 4].

Schamroth's window test performed revealed intact but smaller rhomboid shaped space between finger nail beds, suggestive of moderate clubbing [Figure 5].

Intraoral examination revealed completely edentulous maxillary and mandibular arch, thickened



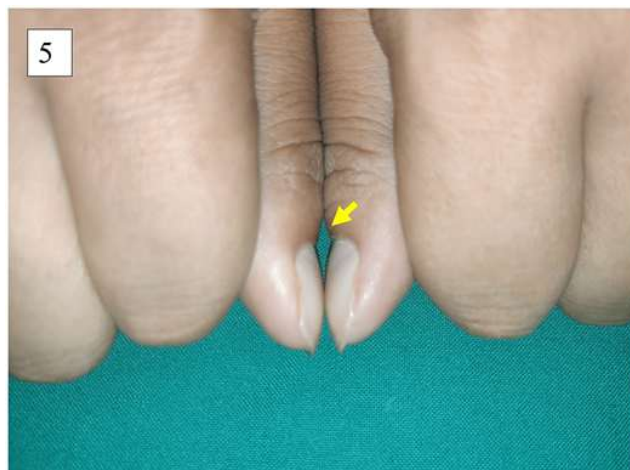
**Figure 2:** A) Extraoral examination revealed dryness and discrete hyperpigmented papules on forehead skin, B) sparse hair and severe recession of hair line.



**Figure 3:** Extraoral examination of his legs revealed a flat spoon shaped nail bed on his left leg.



**Figure 4:** Extraoral examination revealed convexity of nail beds on all his finger digits and increased dryness and pigmentation on the extensor surface of his hands.



**Figure 5:** Schamroth window test or schamroth's sign revealed reduced diamond-shaped space between nailbeds suggestive of moderate clubbing of finger digits.

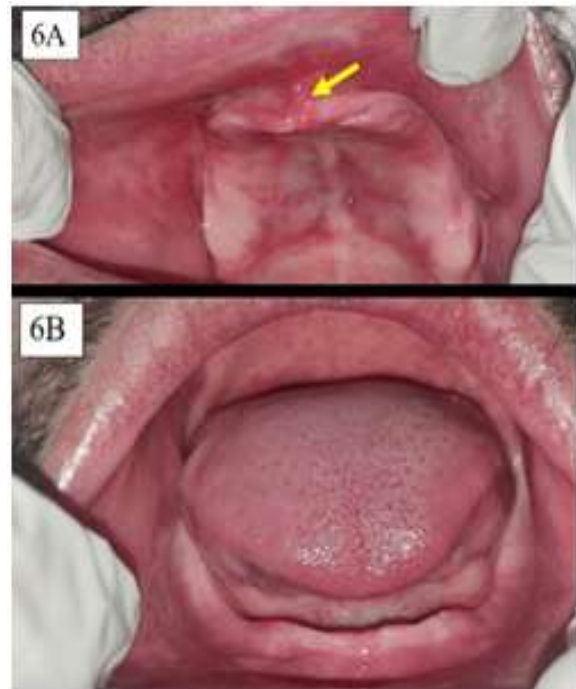
maxillary labial frenum attached near the crest of edentulous maxillary alveolar ridge [Figure 6 A, B].

The removable complete denture prosthesis was fabricated to restore tooth loss and improve masticatory efficiency [Figure 7 A, B].

The differential diagnosis of various syndromes associated with Ectodermal dysplasia is described [Table 1].

### DEFINITION:

EDs form a multisystem genetic disorder with dental defects characterized by a diversified heterogeneous developmental defect in one or more structures of ectodermal origin, one of which involves teeth, hairs, nails, or sweat glands. Other organs derived from ectodermal derivatives include structures



**Figure 6:** A) Intraoral examination revealed thickened maxillary labial frenum and completely edentulous maxilla B) completely edentulous mandibular arch.



**Figure 7: A, B)** The completely edentulous maxilla and mandibular arch were rehabilitated with removable complete denture prosthesis.

**Table 1:** Syndromes associated with Ectodermal dysplasia.

Syndromes with Ectodermal dysplasia	Clinical features
Clouston syndrome	Dystrophy of Nails, Palmo-plantar Hyperkeratosis, alopecia (Partial or Total), Hypotrichosis.
Christ-Siemens-Touraine syndrome	Hypodontia, hypohidrosis hypotrichosis, onychodysplasia.
Ectrodactyly-Ectodermal dysplasia-clefting syndrome (EEC)	Ectrodactyly (split hand and foot deformity), Ectodermal dysplasia (defects of the hair, teeth, nails, and sweat glands), and altered nasal phonation due to Cleft lip/palate (EEC), hearing difficulty due to nasolacrimal ductus agenesis.
Ankyloblepharon Ectodermal dysplasia-Clefting (AEC) syndrome or Hay-Wells syndrome	Ankyloblepharon Ectodermal defects, Cleft lip/palate (AEC)
Rieger syndrome	A Mesoectodermal dysplasia of the cornea and iris, missing teeth, peg laterals, enamel hypoplasia, short dilacerated roots, hyperplastic maxillary labial frenum, malocclusion, microdontia in some cases short stature, abnormal external ears, hypertelorism, mental retardation in some cases, kyphosis, scoliosis, arachnodactyly, polydactyly, imperforate anus, umbilical hernia, myopathy.
Rapp Hodgkin syndrome	Ectodermal dysplasia, hypodontia, cleft lip and palate, scalp dermatitis, hypospadias

of the central nervous system, mammary glands, adrenal, pituitary endocrine glands, meibomian glands, external ear, melanocytes, cornea, conjunctiva, and exocrine glands of lacrimal apparatus<sup>[6]</sup>.

### Synonyms:

Ectodermal dysplasia syndrome, Hereditary ectodermal dysplasia.

### Epidemiology:

The incidence of ED is about 7 per 10,000 live births. The x-linked mode of inheritance is commonly seen among males as the fathers do not transmit to their sons<sup>[7]</sup>.

### Etiology, Genes:

Mutations in the Ectodysplasin A (EDA), Ectodysplasin A Receptor (EDAR), or EDAR associated Death Domain protein (EDARADD) gene located on the long arm (q) of the X chromosome between positions 12 and 13, 2q11-q13, 1q43 respectively prevent mutual mesoderm and ectodermal interactions and affect the usual regular development of teeth, hair, sweat glands resulting in clinical

manifestations of sparse or loss of hair, hypohidrosis, intolerance to heat, anodontia or oligodontia. Other genes involved in the etiopathogenesis of ectodermal dysplasia include the Gap Junction Protein beta-6 (GJB6) gene mapped to chromosome 13q, which encodes for connexin-30. Mutations of the Polio Virus Receptor related-1 (PVRL-1) gene, which encodes a cell-cell adhesion molecule or herpesvirus receptor have been reported in those cases of cleft lip/ cleft palate ED. Mutations in Muscle Segment Homeobox genes (MSX1) cause autosomal dominant tooth agenesis primarily of second premolars and third molars. Mutations in the Paired Box gene 9 (PAX9) transcription factor result in maxillary and mandibular second molar tooth agenesis and oligodontia. Wingless related integration site (Wnt) signaling regulator Axin-related inhibition protein 2 (AXIN2) gene mutations were causative for oligodontia due to missing incisors and predisposition to colorectal cancer<sup>(8)</sup>.

### MODE OF INHERITANCE:

The hypohidrotic type of ED has several forms of heterogeneous patterns of inheritance with variable clinical expressions. The majority are caused by mutations in EDA gene, which are inherited in a X



gender chromosome-linked recessive pattern in which the altered gene is present on the X gender chromosome. In males with only one gender X chromosome, a lone standing mutated gene in each cell is sufficient to cause the condition. Mutated gene results from mutation must be in either copy of the female X- chromosomes to cause the disorder. Females are less affected by gender-linked (X-linked) recessive disorders than males. A remarkable feature of gender-X chromosome-linked inheritance is that males cannot transmit X-linked quality of character to their male siblings. In the gender X-linked recessive form of inheritance, a carrier is a female with a single mutated gene in each germ cell. In about seventy percent of cases, female carriers of hypohidrotic ED experience some clinical features of this disorder. These clinical signs and symptoms are usually mild and include oligodontia or hypodontia or abnormal malformed teeth resembling tapered conical or peg-shaped anterior teeth, molars with the smaller mesiodistal diameter with taurodontism (enlarged pulp chambers) sparse, the lowered density of hair or absence of hair and some problems with the function of sweat glands. The partial expression of an abnormal mutated gene shown by affected females includes hypodontia, oligodontia (teeth reduced in number), or may have mild morphological tooth alterations such as tapered or conical pointed incisors, molars with smaller mesiodistal diameter, or taurodontism (elongated pulp chambers). The incomplete clinical presentation in females is explained by the Lyon hypothesis, which states one X-chromosome in females gets inactive early during embryonic development. so only half of the X-chromosome expresses an unaffected gene and the other half expresses a gene, which is mutated and defective. Hypohidrotic variant can also rarely result from EDARADD or EDAR genetic mutations. An autosomal dominant or recessive mode of inheritance is associated with mutations of EDAR gene, and mutations in EDARADD gene have a pattern of autosomal recessive mode of inheritance. Each cell with a single mutated gene cause ED in autosomal dominant inheritance. Both copies of the mutated gene are altered in each cell in autosomal recessive pattern. Most often in autosomal recessive disorder, the affected person parents with ED do not reveal the clinical symptoms and signs of this disorder, even though they are carry a solitary copy of the altered mutated gene<sup>[9]</sup>.

#### CLASSIFICATION:

Freire-Maia and Pinheiro (1977) classified ED

according to clinical features and associated located areas of developmental defects (1-4) such as 1-Hair, 2-nails, 3- the tooth, and 4-sweat glands<sup>[9]</sup>. They divided the ED into two groups namely Group-A if two ectodermal structures such as hair, nails, tooth, or sweat glands are affected, and Group-B, if one ectodermal structure is affected but had other defects of lip, ear, soles, or palms<sup>[10]</sup>.

#### CLINICAL FEATURES:

ED is a heterogeneous hereditary condition in which two or more embryonic ectoderm tissues develop abnormally at the same time. ED is a syndrome when an ectodermal defect is associated with other anomalies and also isolated in which the defect is isolated only affecting structures derived from ectoderm. The prevalent variants of ED are hypohidrotic and hidrotic<sup>[11]</sup>. Different types of clinical manifestations of hair vary from fine, and short to complete baldness and sparse or complete loss of eyebrow hairs. According to this present case report, our patient has clinical similarities of ED with hair manifestations that include severe recession of the hairline, scant scalp hairs, hairs on the mustache and beard are not affected, and absent eyebrow lashes<sup>[11]</sup>. Saddle noses, depressed nasal bridges, and thick coarse lips are common manifestations. Delayed eruption of permanent teeth, Complete loss of teeth (anodontia), oligodontia, and peg-shaped or conical teeth are some of the dental manifestations of this disease<sup>[11]</sup>. Our case exhibits similar extraoral and intraoral clinical manifestations, including a flat depressed sunken nasal bridge and coarse, thick lips, xerostomia due to salivary gland hypoplasia elicited by stick sign (mouth mirror sticks to the buccal or labial mucosa during clinical examination), and partial hypodontia with conical or tapered peg-shaped central incisor teeth<sup>[11]</sup>. Our patient also had excoriated papules, generalized xerosis, and hypohidrosis all over her forehead, nasolabial fold, and face<sup>[12]</sup>. Children affected by hypohidrotic ED can die within first three years of life due to failure to survive due to a variety of complications, such as acute fatal lung infections like pneumonia, and hyperthermia, as a result of lack of thermal regulation. Therefore, newborns and young children should be given special attention by the treating physician. A typical life expectancy is three years after birth<sup>[12]</sup>.

#### DIAGNOSIS:

No diagnostic guidelines or criteria currently exist for hypo hidrotic ED. Hypohidrotic type must be suspected if a patient has (hypotrichosis) sparse hair on the scalp, or body, (hypohidrosis) reduced ability to



**Table 2:** Diagnostic modalities in Ectodermal dysplasia.

Pilocarpine Microneedles-Sweat induction (PM-SI)		Patches contain 100 microneedles and 600 $\mu\text{m}$ long made of water-soluble materials encapsulating pilocarpine nitrate. These microneedles deliver pilocarpine dosage greater than $0.5 \text{ mg/cm}^2$ , which is double dose when compared to conventional iontophoresis and induce sweating. Sweating is either reduced or absent in Ectodermal dysplasia patients.
Skin biopsy	Invasive	Eccrine sweat glands -absent in hypohydrotic Ectodermal dysplasia.
Radiological imaging		
Orthopantomography	Non-invasive	Gross evaluation of number and shape of teeth. Either complete absence of teeth or hypodontia or oligodontia or conical anterior teeth.
Lateral cephalometric radiographs	Non-invasive	Frontal bossing, depressed mid-face/nasal bridge.
Paranasal sinus view (water's view)	Non-invasive	Opacification of the affected maxillary sinus due to recurrent Chronic maxillary sinusitis that occurs in ectodermal dysplasia patients.
Hand-wrist radiographs	Non-invasive	Decreased tubulation of long bones, osteopenia
Limb radiographs	Non-invasive	To detect decreased tubulation occurring in long bones, fracture lines due to osteopenia, and decreased bone density in ectodermal dysplasia.
DEXA (Dual Energy X-ray Absorptiometry)	Non-invasive	Decreased bone mineral density in the Lumbar spine (L1-4)
CBCT (Cone Beam Computed Tomography)	Non-invasive	For measuring compromised airways (oropharynx) in mid-facial hypoplasia, anteroposterior skeletal abnormalities due to maxillary hypoplasia in Ectodermal dysplasia. Laryngopharynx in Laryngitis, recurrent sore throat in Ectodermal dysplasia patients. It also helps to diagnose fine deviation of inferior turbinates that results in chronic maxillary sinus pathologies in ectodermal dysplasia.

sweat, lower than an actual number of teeth (hypodontia) congenital absence of all teeth (true complete anodontia). If teeth are present, they are usually smaller in size, conical, or pegged in shape, (taurodontism) elongated enlarged pulp chambers in comparison equally to root resembling bull-like is more common in molar teeth<sup>[13]</sup>.

**Table 3:** Management of clinical manifestations of Ectodermal dysplasia.

clinical Manifestations of Ectodermal dysplasia	Treatment
Hypotrichosis	Wigs, 3% Minoxidil topical solutions for sparse hair.
Hypohidrosis	Cool environment (e.g., use of an air-conditioner, a spray bottle of water, cool-ventilated vests) Frequent sipping of water stored in water bottles during a Hot Climate • Skin care products such as emollients containing lanolin, liquid paraffin for dry skin (xerosis), moisturizing creams for eczema, and antihistamine-containing calamine lotions for rashes associated with eczema and certain outdoor activities (e.g., swimming)
Hypodontia	Mandibular implant- assisted Overdentures, complete Dentures, Telescopic dentures for maxilla, Implantretained overdentures, and All-on-four Implants were considered for prosthetic rehabilitation depending on whether only a few (oligodontia or hypodontia) or complete loss (anodontia) of teeth. other dental treatment procedure modalities include dental implants, bonding of conical teeth, and or dentures, and Orthodontic movement of malaligned teeth. simple restorations at an early age of 1.5 to 2 years to complex fabrication of dentures at older age greater than 16 years of age. Bonding of conical teeth improves aesthetics and increased masticatory efficiency. • Dental implants have proven successful in the anteriormandibular arch only in children aged greater than seven years of age. Children with hydrotic ectodermal dysplasia need to replace dental prostheses every two and a half years as dental prostheses cannot accommodate increased edentulous spaces as jaw growth is not hampered in ectodermal dysplasia. Dental implants in adults can support aesthetics & function like occlusion and mastication.
Hyposalivation	Therapeutics (e.g., Artificial salivary substitutes containing carboxy methyl cellulose) directed at coating dry mucosa and maintaining oral lubrication, and reducing the risk of dental caries
Dysphagia	Direct implantation of feeding tubes Percutaneous Endoscopic Gastrostomy (PEG) tube in stomach or Nasogastric tube - passed through nose into stomach. Modifications in diet. Endoscopic assisted Surgical dilatation of oesophagus with non-biodegradable Esophageal Stents namely Allimax - Esophageal Stent (ES) Fully covered Esophageal Stent ( Merit Medical Endotek), Boston Scientific's Polyflex Esophageal Stent, WallFlex -fully or partially covered Esophageal Stent and bio-degradable (Self Expandable) SX- Ella-Danis Esophageal Biodegradable Stent,
Dental caries	Decreased salivation increases the risk of dental caries. Fluoride varnishes and Pit and fissure sealants
Dry eyes	Ophthalmic Lubrication with instillation of eye drops containing carboxy methyl cellulose .
Respiratory manifestations	Recurrent fever from respiratory infections like Pneumonia External punging with wet cotton towels placed on the forehead and body wash with moist water-soaked cotton towels for children Breathing difficulty due to asthma in Ectodermal dysplasia patients. use of Nebulizers containing salbutamol, a bronchodilator for difficulty in breathing Referral to allergist or pulmonologist
Solidified cerumen ear wax	Instill 5-10 drops into the ear canal followed by the use of a cotton plug placed near the entrance of the ear canal. cotton plug moistened with Soliwx@ Ear drops is removed after an hour or a day. The procedure is repeated twice daily for seven days which helps in removing cerumen ear wax. Soliwx@ Ear drops NuLife Pharmaceuticals which contains paradichlorobenzene 2.0 % w/w, Benzocaine 2.7 % w/v, chlorbutol 5.0% w/v, Turpentine oil 15.0% w/v, Butylated HydroxyAnisole (B.H.A) Antioxidants. Referral to (Ear,Nose,Throat) ENT physician

## DIAGNOSTIC MODALITIES IN ECTODERMAL DYSPLASIA:

The various diagnostic modalities in ED are categorized as non-invasive, semi-invasive, invasive as per the diagnostic procedures encountered. These are listed [Table 2]<sup>[14]</sup>.

## MANAGEMENT:

The treatment of ED depends on the type of affected exocrine or endocrine organ, and rapid timely intervention is crucial for a successful and effective outcome<sup>[15]</sup>. Exposure to a hot climate should be managed with physical methods of cooling such as drinking cold beverages frequently and wearing cooling vests which aid in ventilating hot air while working out<sup>[15]</sup>. The cosmetic appearance and function of teeth can be improved with early intervention by dental treatment<sup>[15]</sup>. Dental implants, bone grafting, and dental prostheses should be performed under the supervision of a Prosthodontist<sup>[15]</sup>. Topical 3% minoxidil solutions recently have a promising role in increasing the density of sparse hair in ED patients<sup>[15]</sup>. The therapeutic management of xerosis involves topical emollients such as lanolin, and liquid paraffin. In our case, conservative management of the skin was performed with moisturizing cream<sup>[15]</sup>. The patient must be created awareness about the importance of dental care and replacement of missing teeth<sup>[15]</sup>. The various management of clinical manifestations of ectodermal dysplasia are enumerated [Table 3]<sup>[16,17]</sup>.

Future Prenatal Targeted drug therapies, that target neonatal Fc receptors are under Phase II clinical research. The prenatal intraamniotic administration of Fc-EDA, a recombinant Ectodysplasin A1 protein into the amniotic cavity of affected embryos can prevent the disease and not recommended before gestational week 25 due to risk of miscarriages<sup>(18,19)</sup>.

## CONCLUSIONS:

The term ED describes a group of disorders affecting the ectodermal derivatives such as dermal appendages of the skin, exocrine salivary glands, hair, and teeth. This developmental disorder may affect many ectodermal organs and imparts a variety of clinical symptoms. In patients with ED, physiological and psychological development is impaired due to the dysfunction of orofacial structures and unattractive appearance. The importance of primary provider education in detecting this illness as early as possible cannot be overstated. Multidisciplinary treatment involving Pediatricians, dermatologists, dentists, and other health care providers is needed as many body

organs are affected. The condition and the importance of providing timely routine treatment of these individuals must be explained adequately to parents to prevent adverse treatment outcomes in such individuals. The rehabilitation of missing teeth in our case has resulted in the restoration of lost masticatory function, thereby improving masticatory efficiency.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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## INFORMED CONSENT:

Informed consent was obtained from all individuals, or their guardians included in this study.

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## Case Report

# Herpes associated Erythema Multiforme in Young Child- A Case Report

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### ABSTRACT:

Erythema multiforme (EM) is a mucocutaneous disorder that presents clinically as vesiculobullous and ulcerative lesions affecting any part of oral cavity when occurring alone in oral cavity. It can commonly be seen on skin too with typical target like lesions. We present a case of EM in a 9 year old girl who complained of recurring lesions on lip. Based on history, clinical presentation and serological investigations, it was diagnosed as herpes associated Erythema multiforme (HAEM).

This case was very well managed with systemic steroids and it highlights the advantage of gentian violet for mucocutaneous lesions and also immunomodulator as maintenance therapy.

**KEYWORDS:** Erythema multiforme, HAEM, recurrent herpes infection, gentian violet, steroids

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### INTRODUCTION:

Erythema multiforme (EM) is an acute, self-limited, inflammatory mucocutaneous disease that manifests on skin and often oral mucosa, although other mucosal surfaces such as the genitalia, may also be involved. EM is considered to be a hypersensitivity reaction, and the most common inciting factor is infection, particularly with HSV. Drug reactions to NSAIDs, anticonvulsants or other drugs play a smaller role. It is of four types, EM minor and EM major, stevens jhonson syndrome and toxic epidermal necrolysis. EM generally affects 20-40 years age group, with 20% occurring in children. There may be prodrome of fever, malaise, headache, sore throat, rhinorrhea and cough. The classic skin lesion consist of a central blister or necrosis with concentric rings of variable color around it called typical "target" or "iris" lesion that is pathognomonic of EM.<sup>[1]</sup>

### CASE REPORT :

A 9 year old girl presented to us with history of ulceration and pain in upper and lower lip since 6 days. She had ulcers in the lower lip and tongue since 6 days. Initially ulcer was present only at the corner of mouth which progressively increased and became severe. Oral lesions appeared first followed by one vesicle at right side of face below lip. Oral lesions were associated with pain which increased on mastication (Figure 1).

Past medical history revealed history of ulceration or cracks at the corner of mouth 1 year back in the winter season. Patient was febrile. Right and left submandibular lymph nodes were palpable and tender. No other relevant medical history elicited. Intraoral examination revealed reduced mouth opening. Swelling of upper and lower lips, fissuring and cracking of right and left corners of mouth with haemorrhagic encrustations was noted on right side of

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**Figure 1:** Shows lip lesions on the day patient reported. Note the vesicle on cutaneous part of lower lip.

lower lip (Figure 1). It was tender on palpation. Ulceration was also noted on anterior aspect of tongue and vestibular mucosa. Considering history and clinical examination we arrived at a diagnosis of vesiculo bullous disorder. Differential diagnosis included primary herpes simplex infection, Herpes associated erythema multiforme, Pemphigus vulgaris. Primary herpes was ruled out since classical gingival involvement was absent. Pemphigus vulgaris appears as desquamated areas which represent ruptured roof of vesicle or bulla that does not clinically match. Recurrent HSV infection appears as mild disease but our patient had lesions in multiple areas. So a final diagnosis of EM secondary to recurrent HSV infection (HAEM) was made. Patient was advised routine hematological investigations that revealed normal complete hemogram, peripheral smear and erythrocyte sedimentation rate. Serology tests revealed positive blood titre of HSV antigens and four-fold increase in its antibody.

Patient was advised topical triamcinolone gel (0.1%); topical gentian violet (only for external lip); turmeric based mouthwash (0.1%), systemic prednisolone 30 mg was given in three divided doses that was gradually tapered over a period of two weeks. Multivitamin and antipyretics were also advised on first visit. Maintenance therapy of immunomodulator (Levamisole 150mg) was advised thereafter for a period of 3 months.

Patient was recalled after 3 days, where in patient showed scabbing of lower lip lesion, improved mouth opening, healed tongue ulcers. As per patient's mother, lesion had reduced by 50-60%. Patient was recalled after 5 days that showed 80% improvement and 95% improvement after 10 days (Figure 2).



**Figure 2:** shows significant improvement of lip lesion.

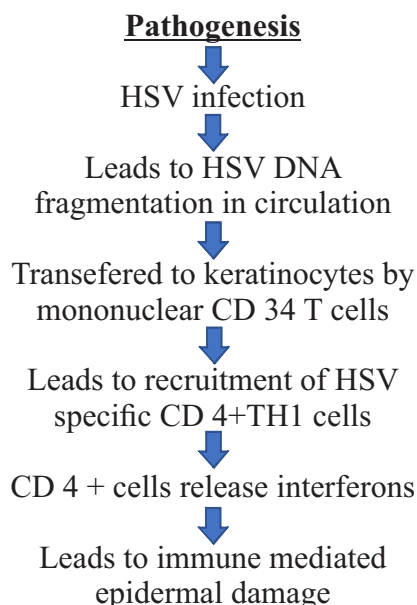
## DISCUSSION:

EM is considered to be acute mucocutaneous hypersensitivity disorder. It is characterized by skin eruptions with or without oral or other mucous membrane lesions. It commonly affects young adults of 20-40 years of age and nearly 20% occur in children. It is more common in females than males. In 70% of cases they have a history of preceding herpes simplex infection.<sup>[1]</sup> It begins as an acute lesion with or without prodromal symptoms. Patient experiences fever, lymphadenopathy, malaise, headache, cough, sorethroat, polyarthralgia, a week before onset of surface erythema or blisters.<sup>[2]</sup> Lesions develop as irregular red macules, papules, vesicles that collapse and gradually increase to form plaques on skin. Skin lesions have a characteristic bulls eye appearance. Oral lesions are referred to as atypical targets. It usually occurs as erythematous macules on lips and buccal mucosa followed by epithelial necrosis, bullae and ulceration with an irregular outline and an erythematous halo. Lip lesions (at vermilion border) are associated with encrustations. EM is of five major types. They are EM minor, EM major, steven Johnson syndrome, toxic epidermal necrolysis and overlap syndrome.<sup>[4]</sup> Herpes associated EM (HAEM) is the kind of EM that is caused by preceding HSV infection.

HSV 1 and 2 have known to precipitate EM.<sup>[1]</sup> HSV DNA has been found in about 60% of patients clinically diagnosed with recurrent HAEM and 50% of patients with recurrent idiopathic EM by polymerase chain reaction.<sup>[5]</sup>

The association between HSV and EM minor was described as early as 1814 by Bateman. Hebra noted it likely occurring in spring and fall when herpetic lesions were common.<sup>[6]</sup> Single episode and recurrent EM patients give a history of preceding herpes infection two weeks or less before onset of disease. Acyclovir is said to be very successful in treating such cases since HSV DNA is detected in about 36-81% of cases.<sup>[1]</sup>

In a study HSV DNA was found in 60% of cases of single episode or recurrent HAEM and also idiopathic EM. Lip is found to be the most common site of preceding HSV infection in case of recurrent EM. Recent study has also found HSV-1 in 66%, HSV-2 in 28% and both HSV-1 and HSV-2 in 6% of the patients.<sup>[1,7]</sup> Half of acute episodes and 80% of recurrent episodes have been associated with HSV.<sup>[8]</sup> Antibodies with precipitin reaction to herpes antigen have been identified in sera of 100% of patients with EM and 50% of EM from other causes. This suggests of presence of occult herpes infection or herpes antigen.<sup>[6]</sup> Delayed hypersensitivity is considered to be the pathogenesis for HAEM<sup>[9,10]</sup> (Figure 3).



**Figure 3:** Flow chart elaborating the pathogenesis of HAEM.

HSV genes can be detected by PCR analysis and immunohistochemistry and reverse transcriptase PCR. Previous history of HSV 1 or 2 infection can be

identified by specific IgM and IgG antibodies for HSV 1 or 2. Presence of specific target like lesions on skin makes the diagnosis easy. Mild form of lesions heal in 2-3 weeks although a wide variety of treatment options are available. Mild form of diseases is usually managed by topical antiseptics, topical steroid gels and pain control can be achieved by analgesics. If patient has fever then antipyretics can be used. Topical gentian violet acts as local antibacterial agents thus prevents secondary infection and aids in healing.<sup>[1,3]</sup>

Lesions can be recurrent in about 20-25% of cases. Since the disease is also termed as self limiting the lesions usually heal in 10-20 days. HAEM can be effectively managed by systemic acyclovir (200mg, 5 times a day for 5 days) along with antipyretics and analgesics. Systemic steroids are preferred in acute cases along with acyclovir for immediate results.<sup>[11]</sup>

Systemic prednisolone 10mg can be given 3 times a day and tapered thereafter. It can also be combined with multivitamins and immunomodulators, especially for maintenance therapy. Mucocutaneous or cutaneous lesions can be treated by topical gentian violet. Since gentian violet has antibacterial properties, it will prevent secondary infection and promote healing.<sup>[11]</sup>

## CONCLUSION:

Erythema multiforme although is a common disease but effective treatment is very important. Our case is important since our patient is young child who presented with HAEM. She was effectively managed by systemic steroids and gentian violet for the vermilion lesions. Immunomodulators can be used to prevent recurrence in cases of HAEM.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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## Research Article

# Prevalence and Correlation of Oral Potentially Malignant Disorder Among Tobacco and Arecanut Users in Gwalior District

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### ABSTRACT:

**Background-** Oral cancer can arise from potentially malignant illnesses through a series of stages, including genetic, epigenetic, and metabolic changes. Some risk factors that increase the risk of developing oral cancer include using tobacco products, especially smokeless tobacco (SLT). The aim of this study was to find correlation & prevalence of oral potentially malignant disorder in tobacco and areca nut user's people residing in Gwalior district.

**Materials & Methods-** A cross-sectional study with a descriptive design was carried out on 3042 participants. The study participants were selected from screening camps and in a hospital environment using simple random sampling. A survey was conducted to gather information on sociodemographic traits, different risk factors for oral cancer, and the existence of the disease's symptoms. The research investigator thoroughly examined each participant's oral cavity in accordance with WHO criteria for the early detection of OPMD.

**Results-** the prevalence of OPMD was 4.27% among tobacco users. OSMF accounted for 1.58% of all cases. Tobacco users had a 3.241-fold increased incidence of OPMD (CI: 0.041-0.303, p=0.01). The consumption of areca nut has increases the incidence of OPMD by 7.17 (CI: 0.747-6.503, p=0.001) times. Alcohol raises the risk of OPMD by 1.51 (CI: 0.002-0.128, p=0.05) times. Males had a 2.54 (1.10-2.42, p=0.01) times increased chance of getting OPMD. Age group 18-30 showed 1.84 (1.32-2.15, p=0.001) times higher chance of developing OPMD.

**Conclusion-** The research reaffirms that the usage of drugs including alcohol, tobacco, and areca nut is one of the modifiable risk factors for OPML.

**KEYWORDS:** OPMD, Tobacco, Oral cancer, Risk factors, areca nut, Smokeless

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### INTRODUCTION:

Oral mucosal abnormalities that are linked to a statistically significant risk of developing oral cancer are referred to as OPMDs. OPMDs may be defined as "any oral mucosal abnormality that is associated with a statistically increased risk of developing oral cancer".<sup>[1]</sup>

OPMDs are characterized by a variety of clinical features, including color variations (white, red, and mixed white-red), morphological modifications (plaque/plateau, smooth, grooved, wrinkled, granular, atrophic), and varying diameters affecting various oral cavity anatomical regions. Remarkably, not every oral

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lesion progresses to become mouth cancer and certain oral malignancies originate from non-dysplastic lesions.<sup>[2,3]</sup> There are currently recognized OPMDs such as discoid lupus erythematosus, actinic cheilitis, leukoplakia, erythroplakia, oral lichen planus, oral submucous fibrosis, palatal lesions of reverse cigar smoking, and some inherited disorders like dyskeratosis congenita and Fanconi's anaemia that are linked to a high risk of malignant transformation.<sup>[4]</sup> Oral cancer can arise from potentially malignant illnesses through a series of stages, including genetic, epigenetic, and metabolic changes.<sup>[5]</sup>

According to epidemiological research, 4.47% of people worldwide may have OPMDs. Of them, the South Asian population has been reported to have the most cases. In Asian populations, the overall prevalence of OPMDs was 10.54%, while in North American groups, it was 0.11%. Non-homogeneous oral leukoplakia (0.16%) was the least common lesion, whereas oral submucous fibrosis (4.96%) was the most common. According to estimates from several research, the frequency of OPMDs varies among populations and is mostly related to lifestyle. Approximately 80% of cases of oral cancer are the result of OPMDs. 7.9% is the total malignant transformation (MT) rate for OPMDs.<sup>[6,7,8]</sup> Oral potentially malignant disorders (PMDs) are quite high in Indian population. According to studies a prevalence rate of 13.2%–13.9% has been observed.<sup>[9]</sup>

Some risk factors that increase the risk of developing oral cancer include using tobacco products, especially smokeless tobacco (SLT), chewing betel leaves, drinking too much alcohol, maintaining poor dental hygiene, eating a diet low in nutrients, and having ongoing viral infections, such as the human papillomavirus (HPV). The global prevalence varies widely, and risk factors related to behaviour, exposure to harsh environments, and lacks of understanding are indicative of this diversity.<sup>[10]</sup> Especially in developing countries, tobacco use (in any form) is one of the main causes of cancer. In addition to tobacco, one of the main causes of mouth cancer is chewing paan, which is made of piper betel leaves combined with areca nut, lime, catechu, cinnamon, etc. The northeastern regions of India have the highest rate of cancer in the country.<sup>[11]</sup>

While there is a paucity of epidemiologic studies that offer valuable insights into the incidence,

prevalence, and severity of oral disease in a particular population, there is a dearth of literature on the prevalence of oral potentially malignant disorders among tobacco and areca nut users in central India. Taking this into consideration, the aim of this study was to find correlation & prevalence of oral potentially malignant disorder in tobacco and areca nut user's people residing in Gwalior district, in order to create a trustworthy baseline data for the development of preventive oral health programmes.

## MATERIALS & METHODS:

The present descriptive-cross sectional study was conducted in Gwalior district. The district has seven tehsils/taluk. For the collection of data we have organized screening camps at each taluk of Gwalior district and we also included the OPD patient of department of oral pathology & microbiology, MPCD & RC, Gwalior MP. Patients diagnosed with oral potentially malignant disorder and having habit of tobacco and areca nut were included in the study. This study has been approved by the Institutional Ethical Committee. Prior to assessment, informed consent from the study participants was taken.

Based on the findings of the pilot study and considering world case scenario we calculated 3042 sample size at 95% confidence interval. Simple random sampling was used for selection of study participants in a hospital setting and from screening camps. The standardized interviewer-based questionnaire was used to record information about the type of habit, duration, frequency, placement site, period of contact with the mucosa, and history of quitting the habit in addition to the patient's demographic details (Name, Age, Gender, Religion, Address, and Socioeconomic Background). A detailed clinical visual examination of the oral cavity especially the lesions involving buccal mucosa, hard & soft palate and tongue along with detailed relevant medical and lifestyle history was recorded. WHO criteria was followed for the diagnosis of each lesion.

Statistical analysis was done using Statistical Package of Social Science (SPSS Version 25; Chicago Inc., USA). Data comparison was done by applying specific statistical tests to find out the statistical significance of the comparisons. Chi square test was used to find significant association between smoking tobacco, chewing tobacco and a combination of both with oral potential malignant disorder. Logistic regression analysis was conducted to predict the occurrence of OPMD to various risk factors. Significance level was fixed at  $p < 0.05$ .

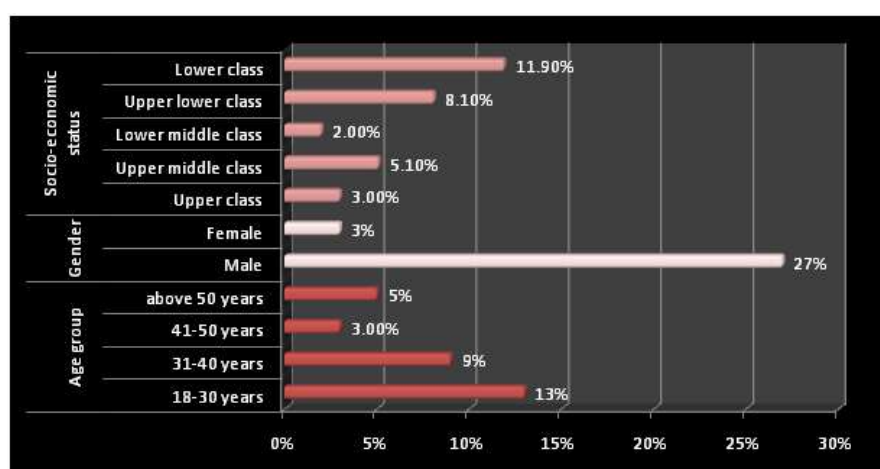
## RESULTS:

There were 3042 participants in all in this study. The study had 34.1% female individuals and 65.9% male participants, with a mean age of 34.86 years. Based on age category, 43% of participants were between the ages of 18 and 30; 27% were between the ages of 31 and 40; 19% were between the ages of 41 and 50; and 11% were over the age of 50. Based on the socioeconomic position of the participants, the majority of them (26.2%) are from the upper lower class, followed by 24% from the lower middle class, 23% from the lower class, 17.9% from the upper middle class, and 8.9% from the upper class (Table 1).

The percentage of individuals who used tobacco was 30% out of 3042, whereas 60% did not use tobacco. A total of 19.0% of individuals reported using smokeless tobacco, 8% reported using smoking tobacco, and 3% reported using both smoking and smokeless tobacco. Based on age group, the majority of participants (13.0%) were tobacco users between the ages of 18 and 30, followed by 9.0% from the age group of 31 to 40. Additionally, 5.0% of participants were above 50, and 3% were from the age range of 41 to 50. Just 3% of the 30% of tobacco users were female, while the bulk of tobacco users (27%) were men. The

**Table 1:** Demographic distribution and personal habit of study participants (n=3042).

Study Variables		n (%)
Mean Age (Mean±SD)		34.86 ±10.80
Age Groups	18-30 years	1309 (43.0%)
	31-40 years	822(27.0%)
	41-50 years	577(19.0%)
	Above 50 years	334(11.0%)
Gender	Male	2006(65.9%)
	Female	1036(34.1%)
Socio economic status (Kuppuswami Scale)	Upper class	272 (8.9%)
	Upper middle class	544(17.9%)
	Lower middle class	729(24%)
	Upper lower class	797(26.2%)
	Lower class	700(23.0%)
Tobacco Use	Yes	913(30%)
	No	2129(70.0%)
Form of tobacco	Smokeless	579(19.0%)
	Smoking	242(8.0%)
	Both	92(3.0%)



**Figure 1:** Distribution of tobacco users according to age, gender and socio-economic status

**Table 2:** Distribution of study participants according to presence of oral potentially malignant disorder (OPMD).

Variable	Tobacco users (n-913)		Non tobacco users (n-2129)	
	Yes	39(4.27%)	0(0.0%)	
Presence of lesion	No	874(95.73%)	2129(100%)	

**Table 3:** Distribution of OPMD according type of disorders.

Type of Oral potentially malignant disorders	Frequency (%)
No OPMD	95.73%
Erythroplakia	0.07%
Erythro leukoplakia	0.03%
Leukoplakia	0.28%
Oral sub mucous fibrosis	1.58%
Dyskeratosis congenita	0.03%
Smokeless tobacco keratosis	0.52%
Palatal lesion associated with reverse smoking	0.13%
Chronic candidiasis	0.05%
Lichen planus	0.81%
Discoid lupus erythematosus	0.05%
Syphilitic glossitis	0.02%
Acthnic cheilitis (lip)	0.7%

**Table 4:** Association between Oral potentially malignant disorders and associated risk factors.

Variables	Odds ratio	95% Confidence Interval	p-value
Use of tobacco	3.241	0.041 -0.303	0.01*
Use of areca nut	7.176	0.747 -6.503	0.001*
Use of Alcohol	1.517	0.002 -0.128	0.05*

\*statistically significant

majority of participants (11.9%) from lower socioeconomic class (SES) reported using tobacco, followed by upper lower class (8.1%), upper middle class (5.1%), upper class (3.0%), and upper middle class (5.1%) (Figure 1).

Based on how often participants used smokeless tobacco, the majority (45.1%) reported using gutkha, followed by raw tobacco (18.0%), toothpowder (13.8%), snuff (9.0%), tobacco with slaked lime (4.61%), tobacco with pan/quid (4.61%), and tobacco in any other form (4.61%). The most popular location for holding smokeless tobacco in the mouth was the buccal vestibule (49.62%), which was followed by the labial vestibule (18.33%), the floor of the mouth (13.56%), the chew and spit (9.23%), and the swallow (9.23%). In terms of the type of tobacco used for smoking, bidi accounted for 55% of all uses, followed by cigarettes (36%), and other forms of smoking (9%).

The current study indicated that the prevalence of OPMD was 4.27% among tobacco users and 0% among non-users. (Table 2) Oral sub mucosal fibrosis (OSMF) accounted for 1.58% of all cases, with Lichen planus (0.81%), smokeless tobacco keratosis (0.52%), Leukoplakia (0.28%), palatally associated with reverse smoking (0.13%), actinic cheilitis (0.7%), Erythroplakia (0.07%), Chronic candidiasis (0.05%), discoid lupus erythematosus (0.05%), Erythro leukoplakia (0.03%), dyskeratosis congenital (0.03%), and syphilitic glossitis (0.02%) respectively (Table 3).

The incidences of OPMD and tobacco usage are positively correlated. Compared to non-users, tobacco users had a 3.241-fold increased incidence of OPMD (CI-0.041-0.303, p-0.01). The consumption of areca nut has also been found to be strongly linked to OPMD; it increases the incidence of OPMD by 7.17 (CI: 0.747-6.503, p-0.001) times. Alcohol use was also found to be substantially linked to OPMD; it raises the risk of OPMD by 1.51 (CI- 0.002-0.128, p-0.05) times (Table 4).

Gender is also linked to the OPMD. In comparison to females, males had a 2.54 (1.10-2.42, p-0.01) times increased chance of getting OPMD. When compared to age groups below 30, those between the ages of 18 and 30 showed 1.84 (1.32-2.15, p-0.001) times higher chance of developing OPMD (Table 5). When we questioned people if they were aware of the negative effects of tobacco use, 99% said they were, and 1% said they were not.



**Table 5:** Association between Oral potentially malignant disorders and age and gender.

Variables		Odds ratio	95% Confidence Interval	p-value
Gender	Female	1.00		
	Male	2.54	1.10 -2.42	0.01*
Age	More than 30 years	1.00		
	Less than 30 years	1.84	1.32 -2.15	0.001*

## DISCUSSION:

The current study's objective was to ascertain the frequency and association of oral potentially malignant condition in Gwalior district tobacco and areca nut users. Tobacco usage was widespread in India, with 20.3% of women and 47.9% of men using tobacco in one way or another.<sup>[12]</sup> The current study indicated that the prevalence of tobacco use was found to be 30%, similar findings were also reported by Srivastava et al<sup>[13]</sup> and Pahwa et al<sup>[14]</sup> this was primarily motivated by its inexpensive and simple availability of tobacco in India. Numerous factors influence and determine tobacco use like social norms; advertising and the economy; cultural aspects such as acculturation, customs surrounding tobacco use, and the tobacco industry's historical background in different communities; individual factors such as perceptions, self-image, and peers; and environmental factors such as advertising and economics.

In our survey, men used tobacco at a higher rate than women. These results were in line with research by Shrivastava et al,<sup>[13]</sup> Sujatha et al,<sup>[15]</sup> and Behura et al<sup>[16]</sup> that revealed harmful oral practices were more common in men. This discrepancy may be due to the fact that men are more likely than women to have ready access to tobacco products, or it could be because many male vocations demand a significant physical expenditure and a high degree of focus, such as drivers, factory workers etc who work odd hours. This may cause tension, and stress combined with peer pressure may cause the development of bad dental habits. Individuals between the ages of 18 and 30 had higher tobacco addiction rates. Similar results were also reported by Grover et al.<sup>[17]</sup> a notably greater percentage of adolescents who smoked were those whose father or closest friend did. In general, young individuals were more perceptive to criticism from their older brother or best friend than from their parents. They knew that smoking was bad for you in general, but they had no idea of any particular health risks. One significant influencing factor in the decision of young individuals to start using tobacco is peer pressure.

The majority of tobacco users in this study were from lower socioeconomic classes; comparable results were also found in a study by Bhan et al.<sup>(18)</sup> In India, the underprivileged have a higher prevalence of tobacco use and are more exposed to the negative effects of tobacco use. According to a review by Hiscock, people from lower socioeconomic backgrounds tend to smoke more, and their attempts to quit are less likely to be successful. These reasons include: less support from the community, a strong addiction, a lower motivation to quit, a higher chance of not completing behavioural and pharmacological interventions for tobacco quitting, psychological issues like low self-efficacy, and marketing from the tobacco industry.<sup>(19)</sup>

In the current study, the prevalence of OPMD among tobacco users was 4.27%. Oral submucous fibrosis was the most common kind, followed by leukoplakia, smokeless tobacco keratosis, and lichen planus. This is similar to a study done in Karnataka by Pahwa et al. where the prevalence of OPMD was 3.75%. The prevalence of OSMF, leukoplakia, and erythroplakia was 2.60%, 1.22% and 0.04%, in that order. In a related study conducted in Indore, Madhya Pradesh in 2015, Kumar et al<sup>(20)</sup> reported greater rates of lichen planus (1.38%), leukoplakia (4.02%), and OSMF (8.06%), with erythroplakia being the least prevalent OPML (0.24%). In the current study, OPMD was diagnosed in tobacco users of any kind, and consumption of alcohol and areca nuts elevated the risk of developing OPMD. In line with the current study, Pehwa et al.<sup>(14)</sup>, Pimple et al.,<sup>(21)</sup> and Kumar et al.<sup>(20)</sup> noted that all individuals with OPML were found to be tobacco user. The present study reported that the OPMD was more commonly occur in males. These results are consistent with research by Kumar et al.<sup>(20)</sup>, Pimple et al<sup>(21)</sup>. Balsaraf and others<sup>(22)</sup> Additionally, Shivakumar et al<sup>(23)</sup> noted that chewers have a roughly by five times increased risk of developing OPMD compared to non-chewers.

According to our research, using tobacco products in addition to alcohol and areca nuts raises the risk of OPMD. Many malignancies, particularly those

of the mouth and throat, are predisposed to by alcohol. Alcohol usage is associated with an increased risk of cancer, which is dependent on the type of alcohol consumed and how often it is consumed. Like many other research, ours found that chewing BQ on a daily basis was associated with a greater chance of acquiring OPMDs. There was another positive relationship found by Worakhajit et al. <sup>(24)</sup> Kumar S et al. <sup>(20)</sup> Younger age groups had a higher prevalence of OPMD; Pehwa et al. similarly found comparable results. According to our research, men are more likely than women to have OPMD. Pehwa et al. similarly observed comparable findings <sup>(14)</sup>. This is due to the fact that, in contrast to men, female tobacco usage is not socially acceptable in central India.

## CONCLUSION:

There is a chance that oral illnesses with malignant potential will eventually develop into cancer. Oral potentially malignant diseases were reported to be present in 4.27% of cases overall. more common occurrence of oral sub mucous fibrosis in the study population. The use of tobacco products, areca nut, intake of alcohol were found to be a risk factor for emergence of potentially cancerous mouth diseases. Younger age groups and men were shown to be at higher risk. Improved attempts to avoid this condition can be made possible by the identification of these risk factors. Those who have if this problem has already shown, advice to lessen the likelihood of this risk factor exposure, which could stop additional advancement of this illness. Since early intervention is essential to successful prevention, the right actions should be performed in this regard. The current policies for quitting tobacco need to be reviewed and strengthened. In particular, strategies to support smoke-free homes and workplaces, as well as comprehensible anti-tobacco/smokeless advertisements and label warnings should be encouraged. Additionally, school and mass media-based education campaigns that raise awareness of the health risks associated with tobacco use and the advantages of quitting should be supported. It appears vital to empower Indian healthcare professionals to advocate for tobacco cessation. Future research should include more longitudinal studies. Also other etiological factors such as dietary factors, oral hygiene practice and genetic predispositions should be explored.

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## Conflicts of interest

There are no conflicts of interest.

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## Review Article

# The Role of Lasers in Dentistry: Advancements, Applications, and Future Prospects

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### ABSTRACT:

Lasers have revolutionized the practice of dentistry, offering precise and minimally invasive solutions across various dental specialties. This comprehensive review explores the historical evolution, fundamentals, applications, challenges, and future prospects of lasers in dentistry. Beginning with a historical overview, the review discusses the fundamental principles of laser-tissue interaction and the types of lasers commonly used in dental practice. It then delves into the diverse applications of lasers in conservative dentistry, periodontology, oral surgery, endodontics, pediatric dentistry, and orthodontics, highlighting their roles in cavity preparation, soft tissue management, disinfection, and surgical procedures. Despite their numerous advantages, challenges such as cost, learning curve, tissue interaction limitations, and regulatory considerations hinder the widespread adoption of lasers in dentistry. However, ongoing research and technological advancements continue to address these challenges, paving the way for enhanced patient care, improved treatment outcomes, and expanded applications of lasers in dentistry. Overall, lasers represent a promising toolset in modern dentistry, offering clinician's precision, efficiency, and patient comfort in various dental procedures.

**KEYWORDS:** Lasers, Dentistry, laser efficiency, patient care, laser application

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### INTRODUCTION:

Dentistry has long been a field that has embraced technological advancements to enhance patient care, diagnosis, and treatment outcomes. Among these advancements, lasers have emerged as versatile tools with numerous applications in various aspects of dental practice.<sup>[1]</sup> From diagnosis to surgery, lasers offer precision, minimal invasiveness, and improved patient comfort. This comprehensive review explores the role of lasers in dentistry, including their advancements, applications across different dental specialties, current challenges, and future prospects.<sup>[2]</sup>

**Historical Overview of Lasers in Dentistry:** The use of

lasers in dentistry dates back to the 1960s when Miaman first introduced the ruby laser for dental applications. Since then, researchers and practitioners have explored different types of lasers, including carbon dioxide (CO<sub>2</sub>), neodymium-doped yttrium aluminum garnet (Nd:YAG), erbium family (Er:YAG and Er,Cr:YSGG), diode, and argon lasers, among others. Each type offers unique properties, wavelengths, and tissue interactions, making them suitable for specific dental procedures.<sup>[3,4]</sup>

### Mechanism of Lasers:

The mechanism of lasers in dentistry revolves around their ability to generate highly concentrated

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beams of light energy. Different types of lasers are utilized in dentistry, including diode lasers, carbon dioxide (CO<sub>2</sub>) lasers, erbium lasers, and neodymium-doped yttrium aluminum garnet (Nd:YAG) lasers. Each type of laser has specific wavelengths and properties that make it suitable for dental procedures. Lasers used in dentistry emit light at specific wavelengths that are selectively absorbed by different dental tissues. For example, water and hydroxyapatite, the main components of teeth, absorb certain wavelengths of laser light.<sup>[4]</sup>

When laser light interacts with dental tissues, it can have various effects depending on the wavelength and the type of tissue being targeted. These effects include ablation (removal) of soft or hard tissue, coagulation (hemostasis) to control bleeding, and disinfection of the treatment area. Some types of lasers, such as diode lasers and Nd:YAG lasers, have bactericidal properties.<sup>[5]</sup>

### **Fundamentals of Dental Lasers:**

**Laser Tissue Interaction:** Understanding the interaction between laser light and oral tissues is crucial for safe and effective use in dentistry. Depending on the wavelength and tissue characteristics, lasers can be absorbed, scattered, or reflected upon interacting with oral tissues. This interaction results in various therapeutic effects, such as cutting, coagulation, ablation, and photo biomodulation.<sup>[5]</sup>

### **Types of Dental Lasers:**

**Hard Tissue Lasers:** Hard tissue lasers, such as Er:YAG and Er,Cr:YSGG lasers, are primarily used for procedures involving tooth structure, including cavity preparation, caries removal, and enameloplasty. These lasers operate at wavelengths that are highly absorbed by hydroxyapatite, allowing precise and efficient removal of dental hard tissues while minimizing thermal damage to surrounding structures.

**Soft Tissue Lasers:** Soft tissue lasers, including diode, Nd:YAG, and CO<sub>2</sub> lasers, are commonly used for gingival surgery, periodontal therapy, frenectomy, and soft tissue biopsies. These lasers offer excellent hemostatic properties, minimal trauma to adjacent tissues, and reduced postoperative discomfort for patients.<sup>[6]</sup>

**Photobiomodulation Lasers:** Photobiomodulation, also known as low-level laser therapy (LLLT), involves the application of lasers at specific wavelengths to promote tissue healing, reduce inflammation, and alleviate pain. This therapeutic modality has found

applications in treating oral mucositis, temporomandibular joint disorders, and accelerating wound healing after surgical procedures.<sup>[7]</sup>

### **Safety Considerations:**

While lasers offer several advantages in dentistry, their safe and effective use requires adherence to strict safety protocols and appropriate training for dental professionals. Key safety considerations include proper eye protection, patient and operator shielding, adherence to laser safety guidelines, and ongoing education on laser technology and techniques.

### **Applications of Lasers in Dentistry Endodontics:**

**Disinfection and Debridement:** Lasers have emerged as promising adjuncts to conventional endodontic therapy for disinfecting root canals, removing smear layer, and promoting periapical healing. Nd:YAG and Er:YAG lasers effectively eliminate bacteria and debris from root canal systems while minimizing the risk of instrument fracture and canal transportation.<sup>[8]</sup>

**Apical Surgery:** In cases of persistent periapical infections or root canal treatment failures, apical surgery may be indicated to achieve periapical healing and preserve the tooth. CO<sub>2</sub> and erbium lasers offer precise and atraumatic means of performing apicoectomy, root-end resection, and retrograde filling, leading to improved clinical outcomes and reduced postoperative complications.<sup>[9]</sup>

### **Conservative Dentistry:**

**Cavity Preparation and Caries Removal:** Lasers have revolutionized the approach to cavity preparation by offering precise, minimally invasive, and painless alternatives to traditional drilling methods. Er:YAG and Er,Cr:YSGG lasers selectively ablate carious tissues while preserving healthy tooth structure, resulting in improved bond strength and longevity of restorations.<sup>[10]</sup>

**Teeth Whitening:** Laser-assisted teeth whitening procedures, often performed using diode lasers in combination with whitening agents, offer faster and more predictable results compared to traditional bleaching techniques. Laser activation enhances the penetration of whitening agents into enamel, resulting in accelerated and long-lasting whitening effects.

### **Pediatric Dentistry:**

**Behavior Management:** Lasers play a valuable role in pediatric dentistry by offering minimally invasive and

painless alternatives to traditional dental procedures. Laser-assisted cavity preparation, frenectomy, and pulpotomy procedures minimize discomfort and anxiety in pediatric patients, promoting positive dental experiences and long-term oral health.

**Orthodontic Applications:** Lasers are increasingly utilized in orthodontics for soft tissue management, including gingival recontouring, exposure of impacted teeth, and frenectomy to facilitate orthodontic treatment. Diode lasers offer precise and bloodless soft tissue sculpting, enhancing the esthetic and functional outcomes of orthodontic interventions.<sup>[11]</sup>

### Oral Surgery:

**Soft Tissue Procedures:** Lasers have become indispensable in oral surgery for performing soft tissue procedures such as frenectomy, gingivectomy, mucocele excision, and biopsy. Diode lasers offer excellent precision, hemostasis, and patient comfort, making them preferred tools for delicate surgical interventions in the oral cavity.<sup>[12]</sup>

**Osseous Surgery:** Er:YAG and Er,Cr:YSGG lasers are valuable adjuncts in osseous surgery for crown lengthening, peri-implantitis treatment, and osteoplasty. These lasers precisely remove bone tissue with minimal collateral damage, resulting in faster healing, reduced postoperative pain, and preservation of surrounding soft tissues.<sup>[13]</sup>

### Periodontology:

**Soft Tissue Management:** Lasers play a crucial role in periodontal therapy by providing precise and efficient soft tissue ablation, decontamination of periodontal pockets, and biostimulation of gingival tissues. Nd:YAG and diode lasers effectively remove diseased epithelium, bacteria, and calculus while promoting periodontal regeneration and wound healing.<sup>[14]</sup>

**Pocket Disinfection:** The antimicrobial properties of lasers, particularly Nd:YAG and Er:YAG lasers, make them effective tools for decontaminating periodontal pockets and eliminating pathogenic bacteria associated with periodontitis. Laser-assisted periodontal therapy results in improved clinical outcomes, reduced pocket depths, and enhanced attachment levels compared to conventional mechanical debridement alone.<sup>[14]</sup>

### Current Challenges and Limitations:

Despite the numerous advantages of lasers in dentistry, several challenges and limitations hinder their widespread adoption and integration into routine

clinical practice.

- **Cost:** The initial investment and maintenance costs associated with laser systems may be prohibitive for some dental practices, especially in smaller settings or developing countries.<sup>[15]</sup>
- **Learning Curve:** Mastery of laser technology requires comprehensive training, proficiency, and ongoing education, which may pose challenges for dental professionals transitioning from traditional techniques.
- **Tissue Absorption and Penetration:** The efficacy of laser therapy depends on tissue absorption and penetration characteristics, which vary based on the laser wavelength, tissue type, and patient factors.<sup>[15]</sup>
- **Regulatory Considerations:** Compliance with regulatory requirements, safety standards, and scope of practice guidelines governing laser use in dentistry is essential to ensure patient safety and legal compliance.

### Future Prospects of Laser and Emerging Trends:

The future of lasers in dentistry holds great promise with ongoing advancements in technology and research. These developments may lead to enhanced precision and efficiency in procedures, expanding the range of applications to include tissue engineering and regenerative dentistry. Personalized treatment approaches tailored to individual patient characteristics are likely to become more prevalent, while miniaturization and portability could increase accessibility to dental care, especially in underserved areas.<sup>[15]</sup>

Integration with digital dentistry workflows will streamline treatment planning and execution, ensuring more efficient and predictable outcomes. Advancements in safety and biocompatibility will further improve the overall safety profile of laser-based dental procedures. Overall, continued innovation in laser technology is set to revolutionize the field of dentistry, offering patients safer, more effective, and more personalized treatment options.<sup>[15]</sup>

### CONCLUSION:

The integration of lasers into the field of dentistry has ushered in a new era of precision, efficiency, and patient comfort. Throughout this review, we have explored the historical evolution, fundamental principles, diverse applications, current challenges, and future prospects of lasers in dentistry.

From conservative dentistry to oral surgery, lasers have demonstrated their versatility and effectiveness in a wide range of dental procedures. Whether it's cavity preparation, soft tissue management, disinfection, or surgical interventions, lasers offer unparalleled precision, minimal invasiveness, and reduced postoperative discomfort for patients. Moreover, their ability to promote tissue healing and regeneration has expanded their role beyond mere treatment tools to therapeutic modalities for conditions such as mucositis and temporomandibular joint disorders.

Despite the significant advancements and benefits offered by lasers, challenges such as cost, learning curve, tissue interaction limitations, and regulatory considerations persist. However, ongoing research and technological innovations continue to address these challenges, paving the way for broader adoption and integration of lasers into routine dental practice.

As we look to the future, the potential of lasers in dentistry is boundless. With continued advancements in laser technology, education, and research, we can expect to see further improvements in treatment outcomes, expanded applications, and greater accessibility to laser-based dental care. Ultimately, lasers stand as a testament to the relentless pursuit of innovation in dentistry, offering clinicians the tools they need to provide superior patient care in the modern dental landscape.

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## Case Report

# All Lymphadenopathies are not Tubercular

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### ABSTRACT:

Lymphadenopathy refers to swelling of lymph nodes. Submandibular nodes (<1 cm) are often palpable in healthy children and young adults; healthy adults may have palpable inguinal nodes of up to 2 cm, which is considered normal. Lymphadenopathy can be localized or diffuse. Lymphadenopathy may be either primary or secondary manifestation of numerous disorders such as infectious diseases, immunologic diseases, malignant diseases (hematologic or metastatic), etc. In clinical practice, more than two-thirds of patients with lymphadenopathy have nonspecific causes or upper respiratory illnesses (viral or bacterial), others are benign while <1% are malignant. Detailed medical history, clinical examination, along with the lymph node examination, routine & special investigations are done. We report 2 cases of lymphadenopathy which were diagnosed as lymphoma.

**KEYWORDS:** Lymphadenopathy, submandibular nodes, lymphoma, hodgkin

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### INTRODUCTION:

Lymphadenopathy is a term that refers to the swelling of lymph nodes. Approximately, 75% of lymphadenopathies are localized, and around 50% of these occur in the head and neck regions.<sup>[1]</sup> Generalized lymphadenopathy is defined as involvement of  $\geq 2$  non-contiguous lymph node groups and is typically indicative of systemic disease. Localized or regional lymphadenopathy implies involvement of a single anatomic area. Persistent generalized lymphadenopathy is defined as lymph nodes of more than 1 cm in size, in 2 or more areas persisting for 3 or more months. Mostly, benign lymphadenopathies have a non-specific or a reactive etiology while others may be associated with infections.<sup>[2]</sup> Lymphadenopathy may be seen in human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS). Hodgkin lymphoma usually presents in young adults, commonly arises in cervical lymph nodes. More than two-third of

the patients of non-Hodgkin lymphoma present with painless peripheral lymphadenopathy. Waxing and waning episodes of lymphadenopathy, along with other symptoms such as fever, weight loss, or night sweats, can be seen in low-grade lymphoma.

### CASE REPORT -1:

A 43 years old male patient, who was a known case of schizophrenia since 20 years, presented to the hospital with complaints of cough, fever and loss of appetite since 1 month. He was taking regular medicines - tab haloperidol 5mg tds, tab promethazine 25mg tds and tab olanzapine 10mg tds for schizophrenia since 20 years. According to his mother, his appetite was reduced since last 2 years from 4 chapatti per meal (2 meals per day) to 1-2 chapattis per meal (2 meals per day). He was vitally stable, except for temperature of 100°F and on general examination was found to have right axillary (lateral group) and

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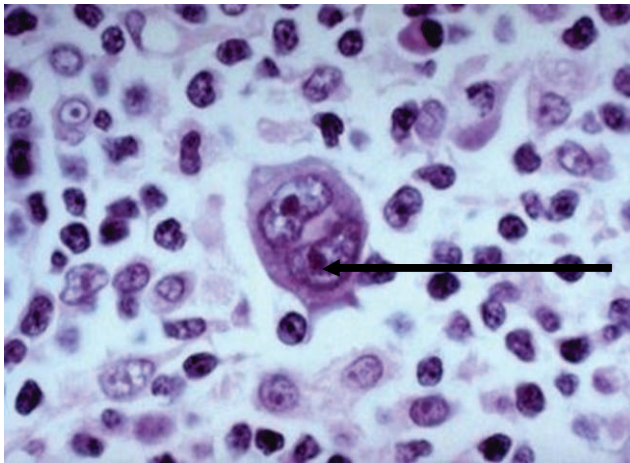
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right epitrochlear lymph node enlargement which were rubbery in consistency, multiple, discrete border, of size 1x0.5 cm and 1.2x1cm, respectively. In systemic examination, all systems were normal. Patient was started on symptomatic and supportive treatment by keeping the differentials as drug-induced lymphadenopathy vs tubercular lymphadenopathy. The investigations were done as follows, complete blood picture with peripheral smear suggestive of microcytic and hypochromic anemia with reactive thrombocytosis. The fine needle aspiration cytology (FNAC) was done which showed clusters of lympho-histiocytes group of cells with entangled atypical cells. There were scattered large atypical cells seen with scant to moderate pale cytoplasm enlarged nucleus, granular chromatin and prominent nucleolus. Focally binucleated, multilobulated 'Reed Sternberg like cells' were also noted with close differential diagnosis of Hodgkin's Lymphoma. Patient was advised biopsy and was referred to higher oncology center for further management but. The patient did not come for any follow-up.



**Figure :** This photograph of histopathological slide shows:- Scattered large atypical cells with scant to moderate pale cytoplasm enlarged nucleus, granular chromatin and prominent nucleolus. Focally binucleated, multilobulated Reed Sternberg like cells are also noted (arrowed).

## CASE REPORT - 2:

A 55 years old male patient came with a complaint of painless swellings below the jaw and in front of the ears bilaterally since 4 months. These swellings were initially of pea size which gradually progressed to current size. There was no discharge. There was no history of fever, weight loss, cough, loss of appetite, no promiscuous behaviour and no history of drug intake. He was a chronic smoker. He was vitally stable and on general examination was found to have right and left submandibular lymph node enlargement which were firm in consistency, discrete border, and

measured 2x1.5cm and 2.5x1.9 cm, respectively. Right and left pre-auricular lymph node enlargements were firm in consistency, discrete border, and measured 1x0.5cm and 1x1.5cm, respectively. In systemic examination, all systems were normal. Patient was started on symptomatic and supportive treatment by keeping the following differentials in mind like immunocompromised status as vs tubercular lymphadenopathy. Patient's sample was sent for all routine investigations and HIV test. He was non-reactive for HIV. FNAC showed scattered monomorphic atypical, lymphocytes (High N: C ratio) mixed with variable cells including macrophage and histiocytes; this was suggestive of lymphoproliferative neoplasm possibly Non-Hodgkin's Lymphoma. Patient was advised biopsy and was referred to higher oncology center for further management. The patient did not come for follow-up.

## DISCUSSION:

Solid tumors of the immune system are Lymphomas and they include 14% of all head and neck malignancies.<sup>[3]</sup> Hodgkin's lymphoma (HL) is a malignancy of mature B lymphocytes. It represents ~ 10% of all lymphomas diagnosed each year. The majority of HL diagnoses are classical HL (cHL), but there is a second subtype of HL, nodular lymphocyte-predominant HL (NLPHL). A bimodal distribution of age at diagnosis has been observed, with one peak incidence occurring in patients in their twenties and the other in those in their eighties. Typical presentations - most patients with cHL present with asymptomatic lymphadenopathy or a mass on chest radiograph. Pel-Ebstein fever is a rare condition reported in patients with HL, characterized by cyclic fevers that rise and fall every one or two weeks. B symptoms are found and they are formally defined as follows: Fever with persistent temperature  $>38^{\circ}\text{C}$  ( $>100.4^{\circ}\text{F}$ ), sweats (presence of drenching night sweats), and weight loss (unexplained loss of  $>10$  percent of body weight over the past six months). The diagnosis of HL is established by review of an adequate biopsy specimen by an expert hematopathologist.<sup>[4]</sup> Non-Hodgkin's lymphomas (NHL) are cancers of mature B, T, and natural killer (NK) cells. They were distinguished from Hodgkin's lymphoma (HL) upon recognition of the Reed-Sternberg (RS) cell and differ from HL with respect to their biologic behaviour. The investigations should include a complete blood count, routine chemistries, liver function tests, and serum protein electrophoresis to document the presence of circulating monoclonal

paraproteins. Lymphoma histopathology and clinical presentation dictate which imaging studies should be ordered. Chest, abdominal, and pelvic computed tomography (CT) scans are essential for accurate staging to assess lymphadenopathy for indolent lymphomas, whereas positron emission tomography (PET) using 18F-fluorodeoxyglucose (FDG-PET) is useful for aggressive lymphomas. The management of NHL affecting head and neck relies on the Ann Arbor staging by an expert hemato-oncologist.<sup>[5]</sup>

Singh Rohit et al reported that, cervical lymphadenopathy is the most frequent head and neck presentation in NHL characterized by multiple painless nodes. These lesions are not as hard as metastatic nodules and are not fixed to either skin or the deep planes.<sup>[6]</sup> In our case, along with cervical lymphadenopathy we found preauricular lymphadenopathy also.

Andrea Gallamini et al found that, HL clinical presentation typically starts with lymph node enlargement, in absence of any subjective symptom or other concomitant clinical signs. Patients seek medical advice because of an enlarged, painless, palpable lymph node, which sometimes shows spontaneous fluctuations of size, more frequently in the upper or lower cervical area (60% of the cases). Other less frequently involved areas are mediastinal (20%), inguinal (7%), axillary (5%) and other (8%).<sup>[7]</sup> In our case, we did not find cervical lymphadenopathy, instead we found right axillary (lateral group) and right epitrochlear lymphadenopathy. This presentation is quite rare. FNAC was carried out. In the first case prominent Reed Sternberg cells were observed. This cell is characteristic of Hodgkin's disease.<sup>[8]</sup>

## CONCLUSION:

We conclude that in patients with lymphadenopathy, the patient's age along with a detailed medical history, drug history and clinical examination are essential, for the proper further work-up including laboratory tests, radiological modalities, and tissue diagnosis, to clinch the final diagnosis. The lymphomas can have diverse kind of presentation so along with medical history the fine needle aspiration and tissue study play an important role.

### Declaration of patient consent:-

The authors certify that they have obtained all appropriate patient consent for his/her/their images and other clinical information to be reported. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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## Short Communication

# Tumor-Specific Immunity: The Promise of Cancer Vaccines

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### ABSTRACT:

Cancer vaccines are a potentially effective way to improve the effectiveness of cancer immunotherapy. They are designed to elicit tumor-specific cellular immunity by antigen presentation by dendritic cells. Tumor-associated antigens (TAAs) have been given top priority by the National Cancer Institute as targets for cancer vaccines. AIA stands for "Adoptive Immune Activation." This approach involves transferring immune cells that have been activated and expanded outside the body back into the patient to target and eliminate cancer cells. The AIA took into account a number of parameters, including therapeutic efficacy, immunogenicity, carcinogenicity, specificity, expression level, and positive cell rate. The spectrum of cancer vaccines is delved in this paper, which covers their creation, modes of action, clinical uses, and future directions.

**KEYWORDS:** Cancer, vaccines, dendritic cells, tumor-associated antigens, immunogenicity

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### INTRODUCTION:

Despite advances in cancer treatment modalities, including surgery, chemotherapy, and immunotherapy, cancer remains a significant global health burden<sup>1</sup>. Cancer vaccines offer a unique approach by harnessing the body's immune system to recognize and eliminate cancer cells<sup>[2,3]</sup>. This manuscript is intended to discuss the role of cancer vaccines in eliciting tumor-specific immunity and their potential as a promising treatment strategy for various malignancies.

### DEVELOPMENT OF CANCER VACCINES:

The development of cancer vaccines involves the identification and selection of Tumor-associated

antigens (TAAs), which are proteins expressed by cancer cells and recognized by the immune system as foreign antigens<sup>[4]</sup>. TAAs are prioritized based on criteria such as their ability to induce a therapeutic immune response, immunogenicity, specificity to cancer cells, and expression levels. Various vaccine platforms, including peptide-based vaccines, dendritic cell vaccines, and viral vector vaccines, have been explored for their potential to stimulate anti-tumor immunity.

### MECHANISMS OF ACTION:

Cancer vaccines work by stimulating dendritic cells to present tumor antigens to T cells, initiating an

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immune response specifically targeting cancer cells (Figure 1). This process leads to the activation and expansion of cytotoxic T cells, which recognize and destroy cancer cells expressing the targeted antigens<sup>[5]</sup>. Additionally, cancer vaccines may induce the production of tumor-specific antibodies and memory T cells, providing long-lasting immunity against cancer recurrence (Figure 2).

### CLINICAL APPLICATIONS:

Clinical trials evaluating the safety and efficacy of cancer vaccines have shown promising results in various cancer types, including melanoma, prostate cancer, and lung cancer<sup>[6]</sup>. Peptide-based vaccines targeting specific TAAs, such as melanoma-associated antigens or prostate-specific antigens, have demonstrated anti-tumor immune responses and improved patient outcomes<sup>[7]</sup>. Dendritic cell vaccines, which involve the ex vivo loading of dendritic cells with tumor antigens, have also shown efficacy in stimulating anti-tumor immunity in clinical trials<sup>[8]</sup>.

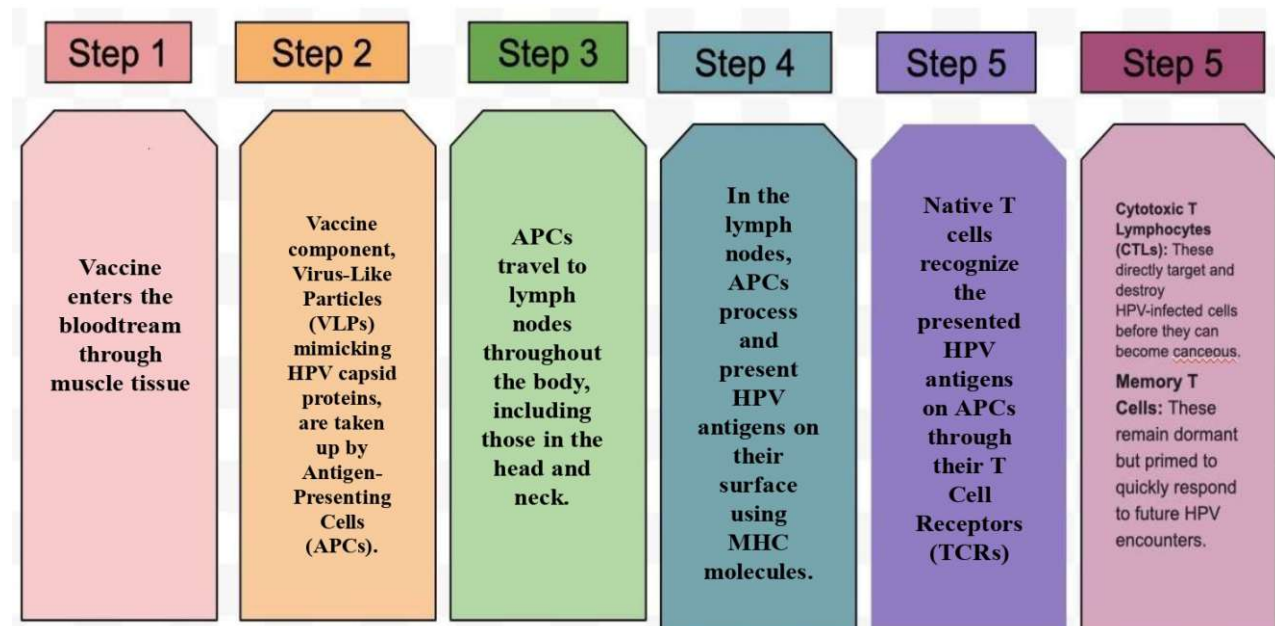
### FUTURE DIRECTIONS:

The future of cancer vaccines lies in optimizing vaccine formulations, identifying novel TAAs, and exploring combination therapies with other immunomodulatory agents. Personalized cancer vaccines tailored to individual patients' tumor profiles



**Figure 1:** Cancer vaccines work by stimulating dendritic cells to present tumor antigens to T cells, initiating an immune response specifically targeting cancer cells.

may enhance treatment efficacy and minimize off-target effects. Furthermore, advances in vaccine delivery systems, adjuvants, and immune monitoring techniques will contribute to the development of more effective cancer vaccines.



**Figure 2 :** Schematic representation of steps of mechanism of action after vaccine administration.

## CONCLUSION:

Cancer vaccines represent a promising approach to harnessing tumor-specific immunity and improving cancer treatment outcomes. By targeting TAAs and stimulating anti-tumor immune responses, cancer vaccines have the potential to complement existing treatment modalities and provide long-term control of cancer progression. Continued research and clinical development are essential to unlock the full potential of cancer vaccines and realize their impact on cancer patient care.

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